"GANN"
THE JAPANESE JOURNAL OF CANCER RESEARCH
VOLUME 30 OCTOBER, 1936 No. 5

原　著 ORIGINALS

Contributions to the Aetiology and Pathogeny of Idiopathic Cystic Dilatation of the Common Bile-duct with Report of Three Cases; A New Aetiological Theory Based on Supposed Unequal Epithelial Proliferation at the Stage of the Physiological Epithelial Occlusion of the Primitive Choledochus

(With 7 Tables, 1 Chart, 3 Figures in the text and Plates XXVIII-XXIX)

By

Syozo Yotuyanagi

From the Pathological Institute of the Tohoku Imperial University in Sendai; Director: Prof. *O. Kimura*)

(Received for publication, August 7th, 1936)

Introduction

Idiopathic cystic dilatation of the common bile-duct was reported for the first time by *Todd* in 1817 in the Dublin Hospital Reports (*McConnel*). Ever since, reports of the disease have been now and again published, but I can find only 145 cases of the disease in original works or in reliable book-reviews throughout the world. According to *Judd & Greene*, 17,381 operations were performed on the biliary tract at the Mayo Clinic from July 1, 1907 to January 1, 1926, yet a true cyst of the common bile-duct was encountered only once. Therefore the disease may be considered as quite rare. In Japan, *Sakuma* was the first to mention a case (1905), and thereafter reports of cases proved by operation or by autopsy amount to 54 (Table I given at the end of this article). Hence the disease is of relative frequency in this land.

I have dissected personally two cases of the disease, which are to be

related in detail. On glancing at the aetiological theories of the disease, I am filled with surprise at their complications. Perhaps, that is due to the fact that having experienced only a few cases — for the most part only one —, authors have maintained their arbitrary opinions based on their personal cases. Therefore the aetiology or pathogeny of the disease seems to me not yet settled.

As the descriptive term of the disease, "idiopathic choledochus cyst" has been used for the longest time and most frequently. Denying the term "cyst", some authors have asserted that "cystic dilatation" was most suitable (*Sato, T., Bohmansson, Lange*), others have kept "cyst", and others have resorted to the appelation "diverticulum" (*McConnel, Reel & Burrell*). Diverticulum means marked dilatation of one side of a tube wall, therefore it can not be applied to all cases of the disease. In the strict sense of the word, "cyst" is certainly not proper, and "cystic dilatation" is most legitimate. Yet the latter means much in the abstract and is not suited to express the dilated portion of the common bile-duct in the concrete. Hence in this article, I will denominate the dilated portion "cyst" — for instance cyst wall.

Report of Personal Cases

Case 1: A boy 2 and a half years of age; autopsy-number 69, 1933.

Clinical History: A boy, aged 2 years and 5 months, the fourth son of a sound farmer, was admitted on the 14th of March, 1933, into the pediatric clinic of the Tohoku Imperial University in Sendai. About the middle of February, 1933, he had been attacked with measles and was before long restored to health. On recovery, his mother noticed that his right epigastrium was abnormally tense. He vomited severely about 10 days prior to his admission and from that time on was inclined to constipation and oliguria.

On examination, the right side of the abdomen was very tense, and a large tumour was found there, but the liver was not palpable. The tumour, cystic and fluctuating, occupied the right hypochondrial region, had a smooth surface and did not adhere to the abdominal wall. A greenish serous fluid containing abundant staphylo-cocci was obtained on stippling. The abdominal circumference amounted to 50 cm at the navel and to 54 cm at the lower margin of the costal arch.

On the second puncture on the 15th of March, about 100 cc of a greenish serous fluid was drawn out, and the albumine-test and *Gmelin*'s test of the latter were strongly positive; on the third puncture on the 20th of the same month, there was the same coloured fluid with fibrinous flocculi, but it contained this time only a few coli-bacilli and pyocyaneus-bacilli. After the third puncture, the tumour enlarged by degrees and came up to the navel. At that time, dilatation of several subcutaneous veins was observed in the epigastrial region, and later the navel projected somewhat. The faeces was coloured greenly and was never acholic. On the 9th of April, the patient vomited coffee-grounds-like substances and died under dyspnoea and cardiac paralysis.

Clinical Diagnosis: Choledochus cyst.

Autopsy Findings: The skin and conjunctiva were quite anaemic and were not at all jaundiced. The abdomen was severely swollen, tense and fluctuating; its circumference amounted to 52.5 cm at the navel, and at the greatest to 57.5 cm. The navel projected like a snout. There were a few slightly dilated subcutaneous veins in the mesogastrial region. A tumour roughly of the size of a child's head was felt in the right side of the abdomen. It was fluctuating and was not sharply contoured.

On opening the abdomen, a large cystic mass which filled up the whole abdominal cavity was found. It was larger than a child's head and was shaped like a gourd with a longer diameter of 22.5 cm; that is the mass, deeply narrowed at its middle portion, was divided into two parts which were spherical in shape. The upper part, 17 : 12 : 12 cm in diameter, which was in the right hypochondrium, reached directly to the anterior margin of the liver and adhered tightly to the hepatic port. The lower part was in the mesogastrium, reached to the promontorium, and was 13.5 : 9.5 : 12 cm in diameter. The tumour was fluctuating, yet its wall felt somewhat firm. The anaemic surface which was covered with serous membrane glimmered through greenly and showed a few slightly dilated blood-vessels. The subserous tissue was oedomatous and seemed somewhat gelatinous.

The dilated gall-bladder, 10 cm in length, was shaped like a banana and extended from the vesical fissure of the liver along the right superior margin of the upper part of the cyst. It adhered tightly to the cyst surface and was covered with serous membrane. On compressing it, its contents flowed easily into the cyst. The liver was severely pushed up, and accordingly the diaphragmatic stand was on

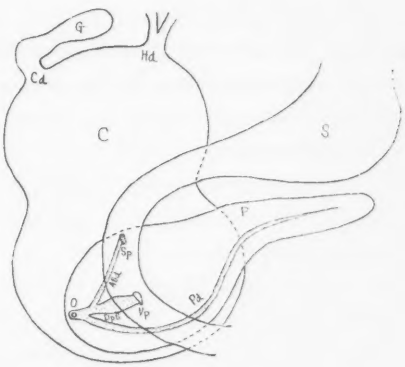


Fig. 1
Schematized Figure of the Cyst of Case 1.
C: cyst. G: gall-bladder. Cd: cystic duct. Hd: common hepatic duct. S: stomach. P: pancreas. Sp: *Santorini*'s papilla. Vp: *Vater*'s papilla. Pd: main pancreatic duct. Dpb: ductus pancreaticobiliosus. Abd: abnormal pancreatic duct. O: orifice of the distal portion of the common bile-duct.

either side at the third intercostal space. The stomach was also pushed up and collapsed, while the small intestines were pressed by the cyst to the left and downward. The transverse colon passed over the cyst surface along the narrowed portion and adhered tightly to the latter. The duodenum, also adhered tightly to the cyst surface, was severely flattened like a belt and was moderately elongated. Its length measured about 19.5 cm, and its width 3.5 cm. At first, it descended from the left side of the upper part of the cyst to the right, crossed with the transverse colon, turned to the left at the middle point of the inferior margin of the lower part and then ascended somewhat. The pancreas was ca. 14.5 cm in length; its head and uncinate process adhered especially tightly to the surface of the lower part and were severely thinned. In other words, the pancreatic tissue spread over the cyst surface in a thin layer and appeared at the right side of the duodenum. Originating from the left side of the narrowed portion, the mesenterial root descended on the cyst surface almost along the left and inferior margins of the lower part. Ca. 25 cc of translucent, slightly icteric fluid collected in the peritoneal cavity.

The cyst contained 1600 cc of greenish, slightly turbid and somewhat mucous fluid. The inside of the cyst was in general smooth, but a moderate number of small shallow holes which were at most lentil-sized could be seen here and there. It was quite anaemic, generally light green, but now and then dark green in colour, and it seemed macroscopically as if it had been covered with a continuous mucous membrane. The cyst wall was roughly 0.2 to 0.3 cm thick and was formed of two layers, namely an outer, thicker, compacter, grayish layer and an inner, thinner, looser, greenish-gray layer.

At the inside, an opening was found at the upper end of the cyst. It was of the size of a pencil, and its anterior margin was somewhat sharpened, suggesting a slight valvular infolding. A probe, introduced into it, came into both hepatic ducts, therefore this opening was the orifice of the common hepatic duct. About 9.5 cm distant from this orifice, another larger opening with no valvular infolding at the margin could be seen. It was large enough to let in a little finger and communicated with the distal end of the banana-shaped gall-bladder. This communicating canal, namely the cystic duct, was moderately dilated and severely shortened. At the lower end of the cyst, no opening could be observed at a glance.

There were two small processes at the posterior wall of the duodenum.

One of them, 6.5 cm distal from the pyloric ring, was in shape and size quite like a clitoris, and its longitudinal axis was laid parallel to that of the duodenum. It was anaemic and free from possible openings. Precisely examined, it was made clear that the process was formed of pancreatic tissue and accordingly was nothing but *Santorini*'s papilla. The other was situated 3 cm further distal from that papilla and was provided with a fissure 1 cm in length. A thin probe, inserted in this fissure, went in the subserous tissue of the cyst wall toward the right and somewhat upward to the extent of several centi-meters and then met with an obstacle. If strongly pushed, it went suddenly into the cyst. Therefore this process must be regarded as *Vater*'s papilla.

By means of inserting a thin probe from *Vater*'s papilla into the inside of the cyst, the orifice of the distal portion of the common bile-duct could be observed at the anterior cyst wall near to the bottom of the lower part. That orifice was very small and of the size of a bougie, yet owing to its great extensibility, it let in a thin probe on strong pushing. Since it had heen covered and hidden by a thin valvular fold formed at its left posterior margin, it could not be found at first without the insertion of a probe.

The distal portion of the common bile-duct in the subserous tissue of the cyst wall was ca. 4 cm in length and was ampullarily dilated at its middle portion — *Vater*'s diverticulum. Its greatest width came to 0.8 cm, and its inside was light green, smooth but not glossy and seemed as if covered with a continuous mucous membrane. At its proximal end, a small opening which led to the inside of the cyst was seen. It was quite round and of the size of a bougie. From this opening, the duct penetrated the cyst wall almost vertically and accordingly opened after the short distance of about 0.5 cm to the cyst. In other words, the distal portion of the common bile-duct originating from the small orifice at the inside of the lower part of the cyst passed through the cyst wall almost vertically, bent at the cyst surface right-angularly to the left and ran in the subserous tissue up to *Vater*'s papilla.

As is shown in Fig. 1, the main pancreatic duct made its way in the thin layer of pancreatic tissue which spread over the cyst surface, and ran parallel with the left and inferior margins of the lower part, crossed with the duodenum, appeared at the right side of the latter and combined at last with the distal portion of the common bile-duct at a point 3.7 cm dis-

tant from *Vater*'s papilla. Therefore the ductus pancreaticobiliosus measured 3.7 cm in length, and the distal portion of the common bile-duct in a narrow sense 0.8 cm. The main pancreatic duct was ca. 17 cm in length and 0.5 cm in width. It contained a translucent, slightly mucous fluid, and its inside was quite anaemic, light green and seemed as if covered with a mucous membrane. On precise examination, a small opening was found at the upper wall of the ductus pancreaticobiliosus. It lay ca. 3.5 cm distant from *Vater*'s papilla and let in only a thin bougie, which was led to blind *Santorini*'s papilla after having passed about 6.2 cm.

The hepatic port was enlarged to the size of a hen's egg. The portal vein adhered to the posterior cyst wall, was flattened like a belt and contained no thrombi, and its intima was quite smooth and glossy.

The liver was slightly enlarged, and the vesical incisure was widened, while the quadrate lobe was thinned. An abnormal lobule of the size of a little finger was seen at the upper part of the latter. The left lobe was yellowish-brown ; the right was spotted now and then dark redly and showed a few dark green speckles which were at most smaller than a lentil. The cut surface was smooth, now yellowish-brown, and now reddish-brown in colour. The acini could be clearly seen, and their peripheral zone was coloured greenly. There were numerous ramified green figures especially in the right lobe, which were nothing else but widened *Glisson*'s capsules imbibed with bile-pigment. Further in the capsules, dilated biliary ducts, filled up with thickened bile, were seen almost constantly.

The pancreas was somewhat smaller than usual ; its surface and also its cut surface were anaemic and showed the so-called lobular structure very distinctly. The lobules were slightly atrophic, and the interstitium somewhat increased in the head and uncinate process.

The stomach was collapsed and contained a small quantity of milky mucous substances. Its mucous membrane was in general pale and rich in folds, and the secretion of slime more or less increased. The duodenum was severely widened and contained only a little grayish mucous substances. Its mucous membrane was quite anaemic, and the folds were indistinctly visible. The small and large intestines contained acholic grayish mucous faeces, and the urinary bladder clear icteric urine.

Post-mortem Diagnosis: Idiopathic cystic dilatation of the common bile-duct. Abnormalities in the course of the pancreatic ducts. Duplication of the left renal pelvis. Abnormal lobule at the quadrate lobe of the liver.

Dilatation of the gall-bladder and cystic duct. Enlargement of the vesical incisure. Dilatation and elongation of the duodenum. Initial biliary cirrhosis of the liver. Initial cholangitic abscesses of the liver. Slight hepatic steatosis. Pancreatic cirrhosis. Slight jaundice of the bilateral kidney. Slight dilatation of subcutaneous veins in the mesogastrial region. Slight oedema of the right leg. Slight dilatation of the right ureter and right renal pelvis. Right severe confluent bronchopneumonia. Grave tracheobronchial catarrh. Severe catarrh of the lymphatic glands in the posterior mediastinum. Interstitial emphysema of the left lung. Acute gastric catarrh. Sclerosis of the thymus. Slight hypertrophia of submucous solitary lymphatic nodules of the small and large intestines. Slight swelling of the mesenterial lymphatic glands. Suppuration of the left eye-lid.

Microscopical Findings: Owing to post-mortem autolysis, it was difficult to stain the inner three-fifths of the cyst wall with haematoxylin-eosin. But by *v. Gieson*'s method, the collagenic fibers were clearly visible in all parts of the wall, and they were loosened in the innermost layer, suggesting submucous tissue. Self-evidently nothing could be seen of the epithelium, the mucous glands and so on. The outer layer consisted of dense fibrous tissue with scanty cells, and its collagenic fibers ran parallel with the cyst wall and sometimes there was slight hyaline degeneration. Although very seldom, a few non-striated muscular fibers could be found between the collagenic; the elastic fibers also were very scanty, were thinned and often knotty. The subserous tissue had turned into similar dense fibrous tissue and was somewhat oedematous.

Glisson's capsules of the liver were widened due to proliferation of the connective tissue in them, and a new-growth of small biliary ducts took place there. Greater biliary ducts were sometimes dilated and often contained amorphous masses of bile-pigment. Now and then, they were filled up with numerous polymorphonuclear leucocytes, which infiltrated over again the duct wall — suppurative cholangitis and pericholangitis. In the capsules, small abscesses with numberless polymorphonuclear leucocytes and coagulated bile could rather frequently be seen. The liver cells contained only a little bile-pigment and had fallen into fatty degeneration in the periphery of the acini. No gall-cylinder. The intratrabecular capillaries were somewhat hyperaemic.

The acini of the pancreas were in general slightly atrophic; the interlobular connective tissue was more or less increased in the neighbourhood

of the head. In the pancreatic tissue which spread over the cyst surface, the interstitium proliferated not only interlobularly, but also periacinarly, and it separated each acinus. Now and then, infiltrations of lymphocytes, mingled with a few leucocytes, were observed there.

The wall of the pancreatic duct which ran on the cyst surface could not be stained because of severe post-mortem alterations.

Case 2[1]: A woman 22 years and 5 months of age; autopsy-number 197, 1929.

Clinical History: A single woman, 22 years and 5 months of age, was admitted on the 16th of December, 1929, into Prof. *Sekiguti*'s surgical clinic of the Tohoku Imperial University under cardinal complaints of abdominal swelling and colic. She was the third daughter of a healthy farmer with no remarkable hereditary relations and had been very weak in infancy. In her 19th year, the menses began, which had been regular up to the date when the first signs of the disease burst out.

In July 1928, the disease declared itself with the following symptoms: slight oedema of the bilateral eye-lid, slight jaundice and itching of the skin, headache and faintness. At that time, she found an ellipsoid movable tumour of the size of a hen's egg in her right hypochondrial region and felt slight pain, on pressure, in the upper part of the navel. She vomited bilious substances several times a day, and the urine was now and then blackish-brown in colour. Since almost all the symptoms were diminished after a week, and since she had never suffered from colic, she did not call a doctor. Meanwhile the tumour enlarged little by little, and by November 1928 it had grown to the size of a goose egg. She was inclined to constipation, and the urine was sometimes grayish-white. Although treated by a doctor for tuberculous peritonitis, she did not recover, but became gradually emaciated, and her abdomon swelled by degrees. In February and in April 1929, she had the tumour in her upper abdomen stippled, and each time ca. 3000 cc of dark green bilious fluid were drawn out. After the punctures, the abdominal swelling decreased, and all her sufferings were lightened for a while. Yet as the days went by, the tumour enlarged again and reached at last to the size of a man's head. She was very much emaciated and had a very poor appetite.

On examination, she appeared to be a girl 14 or 15 years old and was severely emaciated. The skin was pale but was not at all jaundiced. The thoracal organs were compressed severely upwards, and the diaphragmatic stand was abnormally high on both sides. The abdomen was very swollen, as if she had been in the 10th month of pregnancy. The abdominal skin was somewhat glossy because of severe extension, and slight dilatation of several subcutaneous veins could be seen in the neighbourhood of the navel. A tumour, larger than the head of a man, occupied almost the who'e abdominal cavity. It was elliptical in shape, with the greater diameter parallel to the vertebral column, was greatly fluctuating and had a smooth surface with several knolls, and on palpation of its upper part, the patient complained of some pain. The faeces was yellowish-brown in colour, and the urine clear, and the bilirubin-test was in both of them slightly positive.

On the third day after her admittance, she was operated on. The tumour was larger than the head of an adult and filled up the whole abdominal cavity, therefore its contour could not be determined. It was stippled, and ca. 5200 cc of a dark green, faecally

[1] The case was reported by Dr. *Imai*, former assistant in Prof. *Sekiguti*'s surgical clinic, in the Tohoku-Igaku-Zassi, Vol. 17, 1934, P. 99.

stinking fluid were drawn out. The contour became then clearly visible, i. e., two ducts were observed at the upper end of the cyst, and the gall-bladder was situated in the right superior portion of the latter. Cholecystectomy and choledochoduodenostomy were performed.

The fluid, obtained on puncture, was 1032 in specific gravity, contained abundant strepto-cocci and coli-bacilli but no gall-stones, and *Gmelin*'s test of it was strongly positive. The gall-bladder was slightly enlarged and contained but a little thickened bile.

After the operation, the patient felt well for a time, but the pulse soon after became low-tensioned and more frequent, and at last she fell into a collapse. On the following day, she died.

Clinical Diagnosis: Choledochus cyst.

Autopsy Findings: The subcutaneous adipose tissue was highly reduced. The anaemic skin was slightly moist but not at all jaundiced. The abdomen slightly swollen, and a well sutured recent operative wound, 19 cm in length, was seen along the linea alba.

A withered cyst which was almost of the size of a child's head and oval in shape with diameters of 23 : 18 cm came forth beneath the liver. Its surface was for the most part rough, being provided with numberless small fibrous membranes or shreds, and it was brownish-red in colour, moderately hyperaemic and showed several dilated blood-vessels or small haematomata, at most of the size of a cherry. The cyst wall felt firm, and the cyst seemed to contain nothing.

The cyst adhered fibrously in front to the peritoneum of the abdominal wall and on the left to the stomach. Above it was tightly fastened to the hepatic port, from which a tissue strand, several centi-meters in width, descended along the left margin of the cyst to the descending part of the duodenum, adhering loosely to the cyst surface — the hepatoduodenal ligament. The upper part of this ligament had been partially cut off at the time of the operation, and there appeared a duct of the size of a little finger. Originating from the hepatic port, this duct — the dilated hepatic duct — rushed into the cyst obliquely and was narrowed with several sutures near to its entrance

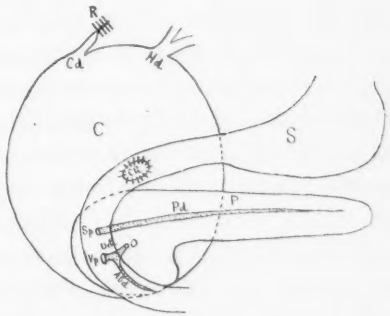


Fig. 2
Schematized Figure of the Cyst of Case 2.
Dch: distal portion of the common bile-duct. Ch: choledochoduodenostomy. R: suture after cholecystectomy. Otherwise as in Figure 1.

into the cyst. The duct contained a dark green muddy bile, and its wall was severely thinned and imbibed with bile-pigment. At the right side of the above stated entrance and ca. 4 cm apart from it, another radiating suture was found. There, according to the statement of the doctor who had operated, the gall-bladder had been combined with the cyst through the somewhat dilated cystic duct. Below the cyst was very tightly adherent to the descending part of the duodenum and also to the pancreatic head and the uncinate process, which was, owing to the pressure of the cyst, so severely flattened that its parenchyma spread over the cyst surface in a thin layer. Further the superior part of the duodenum was sewn on the anterior cyst wall to the extent of a wal-nut in size — choledochoduodenostomy.

The cyst contained only 10 cc of haemorrhagic fluid. The cyst wall was in general 0.3 to 0.6 cm thick, and its cut surface showed two layers, namely an inner, thinner, gray, gelatinous layer and an outer, thicker, tendon-white, fascicular layer. The inside of the cyst was in general grayish and rough and seemed not to be covered with a mucous membrane. Cleaving to the inside, dark brownish-red or brownish-green thick crustaceous substances were observed here and there, especially at the upper half of the cyst.

At the upper end of the cyst, there were two orifices which were ca. 5 cm apart from each other. The left orifice which led to the liver — the orifice of the common bile-duct — was somewhat narrowed by crustaceous substances, while the right — that of the cystic duct — was large enough to let in a little finger. Around this orifice, an anaemic mucous membrane with numerous foveolae was seen to the extent of a cherry in size. Another opening large enough to let in a thumb lay at the anterior cyst wall, but it had only been formed at the operation and communicated with the superior part of the duodenum — choledochoduodenostomy. On careful examination, a pin-head sized orifice was found at the anterior cyst wall near to the lower end. It was quite round, and its margin was smooth, and it seemed as if covered with a mucous membrane. No little scars could be seen either at its margin or in its neighbourhood. A bougie, introduced in this orifice, entered the duodenum without meeting with any hindrances.

At the duodenal wall, *Vater*'s and *Santorini*'s papillae lay in their normal situation and were provided with an opening. A bougie, put in

the pin-head sized orifice at the inside of the cyst, came out from *Vater*'s papilla. In this way, the course and length of the distal portion of the common bile-duct could be learned. That duct was ca. 2 cm in length, and its course was almost vertical to the tangent of the cyst surface and was not at all kinked. If a bougie was inserted in *Vater*'s papilla, it entered now into the inside of the cyst, but it bent now to the left and downward and came into the uncinate process which spread over the cyst surface, i. e., a small abnormal pancreatic duct originating from the uncinate process combined with the distal portion of the common bile-duct to open to *Vater*'s papilla. The main pancreatic duct not combining with that distal portion opened directly to *Santorini*'s papilla.

The liver was normal in size and was slightly pushed up by the cyst. Its surface, also its cut surface was a deeper yellow than usual; the greater biliary ducts were moderately dilated, and their wall was biliously imbibed.

The cut surface of the pancreas was anaemic and showed the lobular structure distinctly. And no marked increase of the interstitium could be observed macroscopically.

The stomach contained but a small quantity of yellowish-brown fluid. The anaemic mucous membrane of the duodenum was coloured somewhat biliously.

Post-mortem Diagnosis: Post-operative state (a recent operative wound along the linea alba, absence of the gall-bladder, choledochoduodenostomy). Idiopathic cystic dilatation of the common bile-duct. Abnormalities in the course of the pancreatic ducts. Initial biliary cirrhosis of the liver. Fatty liver. Lymphatic status. Hypoplastic status. Hypoplasia of the internal genital organs. Hypoplasia of the bilateral suprarenal glands. Abnormal smallness of the aorta. Catarrhalic lymphadenitis of the mesenterial lymphatic glands. Vesicular emphysema of both lungs. Brown atrophy of the heart muscles. Partial fibrous adhesive pleuritis on both sides. Tylosis of the skin in the bilateral subpatellar region.

Microscopical Findings: The tissue structure of the innermost layer of the cyst wall was severely destroyed by haemorrhage accompanied with immigration of numerous polymorphonuclear leucocytes, and the internal surface was deeply ulcered. Hence the epithelium, mucous glands, etc. could no longer be seen in this layer, and small blood-vessels here were frequently thrombosed. Under this layer, there was a narrow zone of typical granulation tissue out of various infiltrating cells, such as leucocytes.

lymphocytes, fibroblasts, etc., and vigorous vascularisation. The outer layer which composed more than half of the cyst wall consisted of dense fibrous tissue with scanty cells. Its collagenic fibers ran parallel to the cyst wall and had partially fallen into hyaline change. In this layer, non-striated muscular fibers were absent, but a few elastic fibers could be seen between the collagenic fibers, and arteries sometimes showed slight hyperplasia of their intima. The subserous tissue was partially covered with fibrin, and the subserous adipose tissue had changed into dense fibrous tissue.

Glisson's capsules of the liver were widened according to proliferation of their connective tissue, and a large quantity of small biliary ducts were formed there. Greater biliary ducts were often dilated and filled up with amorphous masses of bile-pigment. The liver cells contained no bile-pigment and had fallen into severe fatty degeneration in the periphery of the acini. The intertrabecular capillaries were now and then highly hyperaemic.

The pancreas had got into severe post-mortem autolysis, and its interstitium was in general scarcely increased. In the pancreatic tissue spreading over the cyst surface, the connective tissue was strongly proliferated and separated each acinus.

Comments

The reported cases are undoubtedly typical specimens of idiopathic cystic dilatation of the common bile-duct, and the cyst of Case 2 containing 5200 cc of fluid is, together with *Fukuda*'s Case 1, the largest among 54 Japanese cases and belongs to the larger ones among those of all the world —, the largest on record is *Reel* & *Burrell*'s case in which the contents of the cyst amounted to 8000 cc.

In both cases, the orifice of the distal portion of the common bile-duct at the inside of the cyst was very small and showed no considerable cicatrical changes. Because of a marked valvular infolding at the left posterior margin of the orifice, the latter in Case 1 could not be found, until a bougie, introduced in *Vater*'s papilla, came into the inside of the cyst, when it was found to be severely narrowed to the size of a bougie. In Case 2, that orifice was pin-head sized, round and provided with no folds. In this case, the course of the distal portion of the common bile-duct was almost vertical to the tangent of the cyst surface and was not at all kinked. After having passed through the cyst wall vertically at the right side of the duodenum, the distal portion in Case 1 bent at the cyst

surface right-angularly to the left, combined before long with the main pancreatic duct and ran in the subserous tissue of the cyst wall to the left to open finally to *Vater*'s papilla. Such an abnormal course of the distal portion as it lies at the right side of the duodenal papilla has never before been described in the literature and seems at first sight to be a real congenital malformation. As in this case the pancreatic tissue spread over the lower cyst surface in a thin layer, we find that the cyst has enlarged strongly downwards. The valvular infolding at the left posterior margin of the orifice of the distal portion demonstrates to us that the direction of enlargement of the cyst crossed with the primary course of the choledochus and turned more to the right and the front—, the valvular infolding is in general considered as a secondary change caused by this crossing, as is to be mentioned minutely later on. If only the right wall of the common bile-duct had been cystically dilated, then a fold would have been formed at the right margin of that orifice, therefore it must be admitted that the cystic dilatation has taken place on all sides of the choledochus. Since there are some obstacles at the left side of the common bile-duct, such as the greater blood-vessels, vertebral column, etc., every point on the cyst surface, with the exception of the left wall, may move gradually to the right, the front and downward in proportion to the cystic enlargement, and so it should be with the orifice of the distal portion. In this way, the orifice can reach to the right side of the duodenum, and a kinking of the distal portion can be brought about in accordance with the enlarging of the cyst downwards. Thus we are enabled to presume logically that the abnormal course of the distal portion in Case 1 may have been formed secondarily.

The main pancreatic duct in Case 1 made its way on the cyst surface, reached to the right side of the duodenum and combined with the distal portion of the common bile-duct. In the same way as in the distal portion, this abnormality in the course of the pancreatic duct may be explained as a secondary change. In this case, the ductus pancreaticobiliosus was very long — 3.7 cm —, and an abnormal small duct originating from blind *Santorini*'s papilla combined with it. In Case 2, the main pancreatic duct opened to *Santorini*'s papilla, while an abnormal small duct from the uncinate process united with the distal portion of the common bile-duct. These are certainly primary congenital malformations.

Theories Referring to the Aetiology and Pathogeny of Idiopathic Cystic Dilatation of the Common Bile-duct

Concerning the aetiology and pathogeny of idiopathic cystic dilatation of the common bile-duct, all possibilities seem to me to have been pointed out by authors in various theories. In citing them, I prefer to itemize them.

1. Theories in which such dispositions as are acquired post-natally are imputed as a real cause.

A. Tumour in the distal portion of the common bile-duct: *Eve* described a papilloma.

B. Gall-stones or pathological changes of the distal portion due to gall-stones: *Idumi*.

C. Inflammatory process: *Edgeworth* presumed an ascending catarrhalic change which led to stenosis of the distal portion.

D. Trauma which causes weakness of the wall of the common bile-duct: *Kremer*.

2. Theories in which congenital dispositions are imputed as a real cause: *Russell, Exner, Heidecker, Feyrter, Isawa, Kambe, Šantrůček; Nakamura, Igarasi & Fukusima* and others.

A. Obstacle to the biliary outflow due to congenital abnormalities in the course of the distal portion of the common bile-duct.

a) The common bile-duct passes through the duodenal wall in an abnormal direction, namely from left to right instead of from right to left as is usual, and if once biliary stagnation takes place in the proximal portion due to any causes, then a valvular infolding is formed at the inside of the duct at the point where the duct enters the duodenal wall, the biliary stagnation becomes strengthened, and the proximal portion dilates cystically: *Rostouzew, Sternberg, Clairmont, Adam, Wilson, Utida*.

b) Congenital kinking of the distal portion: *Broca, Arnolds, Schloessmann, Seeliger, Fukamati, Kasiwazaki*.

B. *Yasui* reported a case in which the distal portion was divided into two small ducts, and he regarded that malformation to be the primary cause of the disease.

C. *Bakeš* stated that congenital valvular formation in the distal portion obstructed the biliary outflow.

D. Congenital stenosis of the distal portion: *Sakuma, Seeliger, Hayasi; Hill & Ramsay; Zinninger & Cash*.

E. Congenital weakness of the wall of the proximal portion of the common bile-duct of which the former leads to cystic dilatation of that part of the duct: *Goldammer, Kaira, Dreesmann, Lavenson, Mayesima, Takaisi, Yamanouti, Narabayasi, Neugebauer, Kato, K., Kato, R., Karell.*

F. Congenital ampullary, cystic or diverticular dilatation of the proximal portion of the common bile-duct: *Kodumi & Kodama; Waller, Wagner, Flechtenmacher, Budde, Sato, T., Schürholz, Fukuda, Morley, Zipf, Neugebauer, Wright, Young, Lange, Erdély, Kato, R., Oglobin, Giezendanner; Sénèque & Tailhefer; Janik, Saint, Frizelle.*

a) Remembering that the cyst was always formed at the juncture of the hepatic duct with the cystic duct, and that the disease used to be accompanied every time with an abnormal anastomosis between the common bile-duct and the main pancreatic duct, namely an abnormal length of the ductus pancreaticobiliosus, *Kodumi & Kodama* established a peculiar hypothesis. According to them, at the stage when the primitive choledochus indents secondarily from the duodenal wall and unites with the cystic and hepatic ducts, a kinking of the choledochus is brought about at that juncture owing to the fact that the physiological rotation of the stomach, the duodenum, etc. is prevented by the abnormal anastomosis between the common bile-duct and the main pancreatic duct. Then bile stagnates in the proximal portion, and the duct dilates cystically. *Sato, T.* and *Fukuda* endorsed this view.

b) *Budde* at first asserted that a diverticular dilatation was formed due to traction of any aberrant pancreatic tissue in the wall of the common bile-duct, as was also the case in the oesophageal diverticulum.

c) Later he changed his views and stated that a cellular outgrowth of the primitive choledochus, formed by partial luxuriant epithelial proliferation as in the formation of the gall-bladder, became afterwards hollowed and diverticular. In accordance with his "theory of embryological praedetermination of cells in the period of differentiation", *Sebeka* presumed that having got into higher differentiation by mistake, the cells of the primitive choledochus proliferated abundantly and formed a cellular nodule, which afterwards fell into canalisation.

d) *Flechtenmacher, Schürholz* and *Erdély* related that an abnormal budding of the hepatic outpouch developed into a diverticulum, and *Wright* asserted that the rudimentary and additional ducts which were common in human embryos and occurred especially near to the junction of the hepatic

and cystic ducts, and which in general used to be absorbed afterwards, might be encouraged to persist and enlarge up to a cystic dilatation.

G. Theory in which combined congenital malformations, namely an abnormality in the course of the distal portion and a weakness of the wall of the proximal portion of the common bile-duct, are supposed: *Ebner, Kuru, Sugaya, Bolle.*

Criticism on Above

Among all the cases of idiopathic cystic dilatation of the common bile-duct, a genuine tumour was observed only once in the case of *Eve*, therefore *Eve*'s presumption can not be applied to all the cases of that disease. Accordingly such a tumour should be regarded as a mere fortuitous complication and is not the real cause of the disease, although it may be of some significance as an occasional cause, since it may obstruct the biliary outflow.

Idumi could find no gall-stones in the cyst but found several ulcers at its internal surface. Such ulcers were often observed in cases of idiopathic cystic dilatation of the common bile-duct. The first signs of the disease were in *Idumi*'s case somewhat similar to colic due to gall-stones, yet such signs are also pretty frequently described (*Ebner, Sekiguti, Fowler, Flechtenmacher, Melichow, Heidecker, Willis, Erdély*'s Case 1, *Winterstein*). And, what seems curious in collation with constant biliary stagnation and frequent infection of the bilious contents of the cyst, gall-stones generally were very seldom found in the cyst, and any greater than a rice-grain were seen in only 2 among 145 cases (*Sato, T.; Walzel & Weltmann*). Perhaps, that may be ascribable to an early loosening of the epithelial covering at the inside of the cyst wall.

Recently *Virchow*'s hypothesis on the development of catarrhalic jaundice is not in general accepted, therefore it is not advisable to assume that a simple inflammatory process of the common bile-duct causes such a large cystic dilatation.

Trauma may occasion weakness of the wall of the choledochus, however such is a mere conjecture, because it can not be proved actually or objectively. There are only 2 cases with trauma found in the clinical history of 145 cases (*Kremer, Karell*'s Case 2), hence trauma ought to be regarded properly as a mere accidental occurrence.

Since idiopathic cystic dilatation of the common bile-duct occurs predo-

minantly in children and young adults, no one in recent times believes any acquired dispositions to be the real cause of the disease, but every one advocates the theory of congenital malformation.

Rostowzew's hypothesis of abnormal direction of the distal portion of the common bile-duct on entering the duodenal wall has been accepted by many authors and has often been cited in the literature on the subject. But there are not a few objections against his hypothesis (*Lavenson, Waller, Kremer, Schürholz, Zipf, Erdély*). Among them, *Erdély* gave a death-blow to it by asserting that actually the cystic dilatation was not formed immediately touching the duodenal wall, and I hold to this view absolutely. According to my bibliographical studies, the distal, not dilated portion of the common bile-duct was several centi-meters in length in most cases. This fact greatly favours *Erdély*'s opinion and reveals *Rostowzew*'s hypothesis to be a mere academic discussion neglecting the actual facts.

The kinking of the distal portion of the common bile-duct was observed in many cases, and it may result in biliary stagnation. However it may be premature to regard it as a congenital malformation without any consideration of the circumstances, because it can result secondarily from enlargement of the cyst.

Yasui's case is only an exception such as *Eve*'s.

The stenosis of the distal portion of the common bile-duct is very often described in the literature, yet to my surprise, only a few authors correlated it to the cause of the disease. To my mind, that may have happened because of the fact that others regarded simple biliary stagnation due to the stenosis of the distal portion incapable of forming such a cystic dilatation of the proximal portion.

Although weakness of the wall of the choledochus due to hypoplasia or aplasia of the muscular layers and elastic fibers, may be the cause of cystic dilatation of the proximal portion of the duct, no accurate data can be obtained to prove that the hypoplasia or aplasia is congenital in origin (*Erdély*). Others wondered if it might not be somewhat plausible to establish an aetiological hypothesis on assuming hypoplasia or aplasia of muscular fibers, etc., because the common bile-duct contained normally but a few muscular fibers, etc. (*Schloessmann*). In the case of idiopathic cystic dilatation of the common bile-duct, muscular fibers were rather frequently absent or could be found only scattered in the cyst wall. But such a condition can not demonstrate in favour of the hypothesis of congenital weakness,

because it may be brought about secondarily by enlargement of the cyst. On the contrary, the cyst wall was in the case of *Zinninger & Cash* everywhere rich in well developed muscular layers.

According to many authors, the theory of congenital dilatation is based on a sac-like distension of the choledochus in a premature and still-born male foetus related by *Heiliger*. Later, criticism on the various hypotheses as to the congenital dilatation will be made.

Should the Development of Idiopathic Cystic Dilatation of the Common Bile-duct Be Attributable to Many Different Causes or to One?

As already said, there are very many aetiological theories referring to idiopathic cystic dilatation of the common bile-duct, yet on the other hand, we have been able to find certain common features concerning the gross

Table II

Age		Birth–5 yrs.	6–10 yrs.	11–15 yrs.	16–20 yrs.	21–25 yrs.	26–30 yrs.
Male	Actual number	8	7	5	3	4	2
	Percentage	24.2	21.2	15.2	9.1	12.1	6.1
Female	Actual number	20	16	11	11	25	5
	Percentage	19.0	15.2	10.5	10.5	23.8	4.8
Cases with unknown sex		3	2	0	0	0	0
Total	Actual number	31	25	16	14	29	7
	Percentage	21.7	17.5	11.2	9.8	20.3	4.9

31–35 yrs.	36–40 yrs.	41–45 yrs.	46–50 yrs.	51–55 yrs.	56–60 yrs.	61–65 yrs.	66–70 yrs.	Total
1	3	0	0	0	0	0	0	33
3.0	9.1	0	0	0	0	0	0	
4	1	5	3	1	1	1	1	105
3.8	1.0	4.8	2.9	1.0	1.0	1.0	1.0	
0	0	0	0	0	0	0	0	5
5	4	5	3	1	1	1	1	143
3.5	2.8	3.5	2.1	0.7	0.7	0.7	0.7	

pathological anatomy, etc. in the cases of the disease, as is given in the following:

1. The disease occurs selectively in children and young adults. Among 143 cases in which the age is known, 56 (39%) are under 10 years, and 115 (80%) under 25 (Table II). Since the age is reckoned in these statistics from the date of death or the last operation, if it is reckoned from the date of the beginning of the disease, the percentage may become still greater in children and young adults.

2. The disease predominantly attacks females. To take the statistics on 139 cases with known sex, 106 (76%) belong to the female sex (Table III).

Table III

Sex		Japanese cases	Foreign cases	Total
Male	Actual number	18	15	33
	Percentage	35.3	17.0	23.7
Female	Actual number	33	73	106
	Percentage	64.7	83.0	76.3
Total		51	88	139

3. It shows approximate gross anatomical findings. The disease is called generally cystic dilatation of the common bile-duct, yet strictly speaking, the dilatation does not commonly happen only to the common bile-duct. According to the constituents of the cyst, I have classified all the cases of the disease found in the literature into 4 types. In type 1, the cyst is formed of the common bile-duct, cystic and common hepatic ducts, therefore it is provided with two orifices of the cystic and common hepatic ducts at its upper end and with one orifice of the distal portion of the common bile-duct at its lower; in type 2, it is formed of the common bile-duct, cystic and both hepatic ducts, and therefore is provided with three orifices of the cystic and both hepatic ducts at its upper end and with one orifice of the distal portion at its lower; in type 3, it is formed of the common bile-duct, cystic, common hepatic and pancreatic ducts, and therefore is provided with two orifices at its upper end as in type 1 and with two orifices of the distal portion and pancreatic duct at its lower end. Theoretically there may be further a type with three

orifices at the upper end as in type 2 and with two orifices at the lower end as in type 3, but no such case is described in the literature on the subject. In type 4, the cyst is formed merely of the common bile-duct. Among 49 cases with minute descriptions based on autopsy findings or on materials exstirpated at operation, 32 belong to type 1, 11 to type 2, and 3 each to types 3 and 4 (Table IV). Types 1 and 2 may be regarded as

Table IV

Types	Actual number	Percentage
Type 1	32	65.3
Type 2	11	22.4
Type 3	3	6.1
Type 4	3	6.1
Total	49	

being closely approximate to each other, and the total of the two types amounts to 43 among 49 cases.

That all the cases of idiopathic cystic dilatation of the common bile-duct possess certain common features, makes us consider that the cause of that disease ought to be considered as simpler, and the data given in Clause 1 demonstrate that the cause ought to be congenital in origin.

Two Conditions Indispensable to the Development of Idiopathic Cystic Dilatation of the Common Bile-duct, and the Pathogeny of the Disease

If there are in the distal portion of the common bile-duct such hindrances as obstruct the biliary outflow, for instance wedging of gall-stones, cicatrical stenosis, tumour of the duct itself, tumour of adjacent organs that compresses the bile-duct, etc., the proximal biliary tracts dilate in general equally and at most to the size of the small intestine. Studying this problem systematically, *Huber & Lutterotti* rectified this common knowledge. According to them, in the case of the obliteration of the distal portion, the proximal choledochus alone dilates but seldom, actually it was so in only one among their 15 examined cases, and in that case the duct was spindle-shaped with its greatest width 1.5 cm.

In the case of idiopathic cystic dilatation of the common bile-duct, only a limited part of the latter, namely from the junction of the hepatic and cystic ducts to a point several centi-meters distant from *Vater*'s papilla, dilates cystically. Thus, in both cases, of secondary obliteration or stenosis of the distal portion of the common bile-duct on one hand and of idiopathic cystic dilatation on the other, the dilatation of the choledochus differs greatly not only in quantity, but also in quality. Hence in the pathogeny of idiopathic cystic dilatation, a factor which enables the choledochus to dilate partially and also cystically must be required in the first place. To satisfy this demand is the first condition indispensable to the development of the disease.

Theoretically speaking, localized cystic dilatation of the choledochus might occur either through weakness of the duct wall or through congenital dilatation. Although the theory of congenital weakness can not be denied positively, it has never been proved in the concrete, and its establishment seems somewhat unplausible. Furthermore there are cases which disprove it. Hence I may regard the theory to be purely imaginary. Against the theory of congenital dilatation, no counter-evidence has been proposed, and besides, this theory is maintained in several points, as follows: 1. *Heiliger*'s case of a premature male foetus, as mentioned above. 2. There are 4 cases in the literature with marked abdominal swelling at birth (*Oxyley*, *Kawaisi*, *Giezendanner*, *Backer-Grøndahl*'s Case 1), and 2 of them died in less than 4 months after birth (Table V). In these cases, the congenital abdominal

Table V

Author	Age	Sex	Cyst	
			Size	Contents
Oxyley	5 wks.	f.	of the size of a cocoa-nut (at autopsy)	36 oz (on puncture)
Isoda & Kameda	52 days		of the size of a goose egg	
Buzik's Case 2	2 & a half mos.	f.	of the size of a goose egg; 7:7 cm	51 cc (after fixation in formol)
Kawaisi	4 mos.	f.		500 cc
Kuriyama	4 mos.	f.	of the size of a child's head	
Terada & Yagi	4 & a half mos.	m.	10:8:5 cm	120 cc
Bolling	6 mos.	f.		16 oz
Ogawa	6 mos.	f.	14:14:9 cm	1300 cc

swelling ought reasonably to be referred to the congenital dilatation of the common bile-duct. 3. As is shown in Table V, in 8 cases where death occurred in less than 6 months after birth a large cyst was rather frequently found at autopsy. This fact makes us presume that the dilatation may have been in existence very early in life and probably already at birth. From these reasons, I prefer, as a factor to satisfy the first condition, the congenital dilatation to the congenital weakness of the duct wall.

Common sense can scarcely allow us to believe that such large cysts as used to be encountered at operation or at autopsy exist at birth, and indeed in *Heiliger*'s case of a premature foetus the sac-like dilatation measured but 3 : 2.2 cm in diameter. Therefore, only in case of further enlarging, a congenital dilatation of the proximal choledochus which should be considered as one pathological state manifests as one disease presenting certain clinical symptoms such as jaundice, pain and tumour, i. e., the so-called trias of the disease. The enlargement of the congenital dilatation results self-evidently from increase of the internal pressure due to the biliary stagnation. Among 127 cases with minute clinical history, jaundice was observed in 107 (Table VI). Of course, cases with no jaundice can not be

Table VI

Jaundice	Actual number	Percentage
Positive cases	107	84.3
Negative cases	20	15.7
Total	127	

positive counter-evidence against the existence of obstacles to the biliary outflow in them, because stagnated bile may, on some occasions, collect merely in the cyst without having any effect upon the liver. We may, therefore, conclude that idiopathic cystic dilatation of the common bile-duct is almost always accompanied by biliary stagnation.

The second condition indispensable to the development of the disease is a factor which makes a congenital dilatation as one pathological state develop into one disease. And the factor is, of course, nothing but the obstacle to the biliary outflow commonly observed in case of the disease.

Many causes resulting in biliary stagnation may be enumerated, but such as are acquired post-natally ought to be discarded, because the disease

occurs generally in children and young adults. And as congenital causes, we can point out theoretically only two possibilities, namely a congenital abnormal course and congenital stenosis or atresia of the distal portion of the common bile-duct.

As mentioned above, *Rostowzew*'s hypothesis can not be accepted. In the cases of idiopathic cystic dilatation of the common bile-duct, a kinking of the distal portion was often observed, yet no one has proved it to be congenital in origin, and also no one can deny that the distal portion becomes kinked secondarily due to enlargement of the cyst. Therefore many authors regarded it to be a secondary change (*Lavenson, Ebner, Kremer, Schürholz, Zipf, Erdély, Janik*). In case a kinking is found, it must be decided whether it is formed congenitally or secondarily, which can not be determined easily. Yet it may be possible in some cases to understand analytically the mechanism of the formation of a kinking through comparing and contrasting the direction of the cystic enlargement and the localization of a valvular infolding formed at the orifice of the distal portion with the direction of the kinking. If so, the kinking may undoubtedly be a secondary change. But no one has attempted such an analytical study, and those who maintained the theory of congenital kinking did not clarify the grounds on which they stood to their views. In my opinion, among the cases reported by them, such cases as those in which the kinking could be recognized through analytical studies as a secondary change may have been included. On the other hand, there are not infrequently cases with the non-kinked distal portion (*Sakuma, Fowler, Waller, Erdély*'s Case 2, *Isawa, Kiselev*'s Case 1, author's Case 2), therefore the kinking is not indispensable to the development of idiopathic cystic dilatation of the common bile-duct. On these grounds, I can not regard the kinking of the distal portion as satisfying the second condition.

In the cases of idiopathic cystic dilatation of the common bile-duct, stenosis or atresia of the distal portion of the choledochus was very often observed. In order to learn the frequency of their occurrence, I have drawn up Table VII, in which only cases with minute descriptions based on autopsy findings or materials exstirpated at operation are adopted. On glancing at that table, I am astonished to find, beyond my expectation, so many cases with positive stenosis or atresia of the distal choledochus. The distal portion is to some degree narrowed in 42 among 55 cases, namely in 77%, and it is normal-sized in only one. Of course, in the cases with simple

Table VII

Distal portion of the common bile-duct	Birth-5 yrs.	6-10 yrs.	11-15 yrs.	16-20 yrs.	21-25 yrs.	26-30 yrs.	31-35 yrs.	36-40 yrs.	41-45 yrs.	46-50 yrs.	Total
Atresia (can not be seen)	9	6	1	1	0	0	0	0	0	0	17
Severe stenosis	4	0	1	0	1	0	0	0	0	0	6
Moderate stenosis (pin-head sized, smaller than 2 mm in diameter)	3	2	1	0	2	0	0	1	0	1	10
Slight stenosis (passable for a probe, larger than 2 mm in diameter)	0	0	1	1	2	0	0	2	2	1	9
Passable for a probe	1	3	4	1	2	0	0	1	0	0	12
Normal-sized	0	0	0	0	1	0	0	0	0	0	1
Total	17	11	8	3	8	0	0	4	2	2	55

descriptions " passable for a probe ", the distal portion may not be regarded as normal-sized, and there are not a few cases in which the distal portion is slightly narrowed and yet lets in a probe, and indeed it is so in 9 cases under " slight stenosis " in Table VII. These cases with somewhat obscure descriptions being omitted — the total then becomes 43 —, the ratio of the positive stenosis or atresia comes to 97%. Hence it is not too much to say that the stenosis or atresia of the distal portion is an almost constant accompanying phenomenon of idiopathic cystic dilatation of the common bile-duct.

Close observation of Table VII makes us notice that the younger the patient is, the higher is the degree of the stenosis of the distal portion. What does this mean? 1. It shows that the stenosis is congenital in origin[1], because if it is not, the stenosis ought to become severer in proportion to the age. 2. Cases with severe stenosis present serious symptoms in early age and die. In other words, the degree of the stenosis is closely related to the development of certain clinical symptoms and accordingly to the development of the disease, idiopathic cystic dilatation of the common bile-duct.

[1] Atresia of the distal portion is observed in 8 cases older than 5 years (Table VII). It is not plausible in such cases to presume that the atresia is congenital in origin, because if so, the patient could not live for so many years. Hence the atresia must be secondary in origin, yet we must not conclude that the choledochus formed normally comes to be obliterated due to accidental causes which occurred by chance during life, because if so, the atresia should be encountered more commonly in advanced age. In such cases, therefore, the choledochus must have been formed pathologically and indeed narrowly. Thus these two facts, that the atresia is in part secondary in origin, and that the stenosis is in general a congenital malformation — do not run counter to each other.

On these grounds, I look upon the stenosis or atresia of the distal portion as a factor satisfying the second condition indispensable to the development of the disease.

To summarize this chapter, as to the pathogeny of idiopathic cystic dilatation of the common bile-duct, two conditions are demanded. The first condition is the factor which enables the limited part of the choledochus to dilate cystically, and I consider the congenital dilatation of the proximal portion of the duct as satisfying this condition. The second condition is the factor which makes the congenital dilatation as one pathological state develop into one disease, and I consider the congenital stenosis or atresia of the distal portion as satisfying this condition. To my mind, the pathogeny of the disease can be explained, as follows. In the choledochus with these two congenital malformations, bile stagnates owing to the congenital stenosis or atresia and in some cases to certain occasional causes, and then the congenital dilatation becomes enlarged more and more to form at last a large cyst and to cause certain clinical symptoms.

Intimate Relation between Two Diseases, Idiopathic Cystic Dilatation of the Common Bile-duct and Congenital Atresia of the Biliary Tract

As was said in the foregoing chapter, the stenosis or atresia of the distal portion of the choledochus used to be encountered almost constantly in case of idiopathic cystic dilatation of the common bile-duct. *Giezendanner* stated that cases of that disease accompanied by atresia of the distal portion had been described several times in the literature on this subject — it was so with the case of his own —, and he thought that in this case a cystic dilatation of the proximal portion had been in existence at birth, and that the atresia had been brought about post-natally owing to the pathological process explained by *Beneke* as active snaring. *Terada & Yagi* gave similar opinions. These authors did not relate the atresia of the distal portion with the cystic dilatation and regarded both of them as being independent of each other.

Kuriyama stated, on the contrary, that it was interesting to make generalizing observations upon both diseases, namely idiopathic cystic dilatation of the common bile-duct and congenital atresia of the biliary tract, and thus he suggested a vague relation between them. In addition, *Feyrter* affirmed a very intimate relation between them and asserted that it was

possible to unite them pathological-anatomically into one disease, "malformation of the extrahepatic biliary tracts accompanied by disturbance in the formation of their normal cavity — Fehlbildung der extrahepatalen Gallenwege mit Störung der normalen Hohlraumbildung". *Hanser* agreed with him, and I also do absolutely and will argue for his views, as follows: In case of idiopathic cystic dilatation, the distal portion of the common bile-duct is almost constantly narrowed or is often obliterated (1). If only the limited distal portion is obliterated in case of congenital atresia of the biliary tract, the proximal choledochus dilates either slightly (*Skormin*, *Simmonds*'s Case 1, *Elperin*) or somewhat cystically (*Legg*, *Witzel*, *Parker*'s Case 1, *Ylppö*'s Case 2, *Böhm*, *von der Weth*'s Case 2). In the case of the latter, the disease is similar to idiopathic cystic dilatation, and indeed *Giezendanner* included, in his statistical studies, these 6 cases in this disease[1]. *Oxyley*'s case was considered by many authors as idiopathic cystic dilatation, while others reckoned it congenital atresia of the biliary tract. Thus there are many transitional forms between the two diseases (2). Based on these data (1 and 2), we may conclude that both diseases are related intimately with each other, are essentially the same from a pathological-anatomical point of view and accordingly result from the same cause. Therefore it should be possible to apply the aetiological theory of idiopathic cystic dilatation in explanation of the aetiology of congenital atresia of the biliary tract.

Explanation of the Aetiology of Idiopathic Cystic Dilatation of the Common Bile-duct by Means of Supposed Unequal Epithelial Proliferation at the Stage of the Physiological Epithelial Occlusion of the Primitive Choledochus

In the general outline of the developmental data of the liver and extrahepatic biliary tracts, authors agree nowadays with each other (*Hertwig*, *Ghon*, *Fischel*, *Hanser*, *Pfuhl*). According to them, at an early period of the foetal life, an outgrowth in the form of a groove makes its appearance from the ventral wall of the primitive intestinal tube to a somewhat large extent and invades the ventral mesogaster — hepatic outpouch. In two parts of the basis of this outpouch, cells are proliferated, and solid buds out of epithelial cells formed in this way are further extended. The

[1] In my statistical studies, these cases are omitted, because in them the cystic dilatation is not larger than the small intestine, to the size of which the choledochus may dilate in case of secondary obliteration of its distal portion.

cranial bud later makes hepatic parenchyma — pars hepatica —, while the distal bud is responsible for the formation of the gall-bladder and cystic duct — pars cystica. In proportion to the enlargement of the pars hepatica, the hepatic outpouch which was at first wide becomes narrowed into a neck, and thus the primitive choledochus is formed. It is solid at an early stage (according to *Hanser* in a 6.75 mm embryo) and afterwards comes to be cavitied. As to the stage of the solid primitive choledochus, authors disagree in their opinions (*Hanser*). Some stated that the choledochus was solid from the first, and others that it was hollowed at the very first, became solid temporarily due to vigorous proliferation of its epithelial cells — epithelial occlusion — and then obtained a cavity for the second time (*Böhm*, *Rietz* and others).

Comparing these developmental data, I will criticize in this place the theories referring to the congenital dilatation of the common bile-duct which were related in the chapter, "Theories Referring to the Aetiology and Pathogeny etc.". It is self-evident that the theory of *Kodumi & Kodama* is contradictory to our recent developmental knowledge. *Budde*'s theory of aberrant pancreatic germinal tissue has not since been testified to, therefore the existence of that tissue in the cyst wall of his case should be regarded as a mere accidental occurrence. The theories given in Clauses c and d, do not go against our embryological knowledge, but do not explain the development of the congenital stenosis which used to be commonly observed in the distal portion of the choledochus in cases of idiopathic cystic dilatation of the common bile-duct, therefore they are not perfect theories.

Various theories are also proposed as to the aetiology of congenital atresia of the biliary tract. Among them, those in reference to congenital malformation are very cogent, and they can be classified into two groups. 1. The hepatic outpouch is snared in excess, and thus the primitive choledochus is broken: *Benecke* assumed an active snaring due to internal conditions of the cellular life, and *Elperin* a passive snaring affected by certain mechanical powers. 2. In the solid primitive choledochus, a cavity is not formed after all: *Feer*, *Giese*, *Lomer* and others thought that the primitive choledochus which was solid from the very first continued in that state (cited from *Böhm*), while *Böhm*, *Buzik*, *Ylppö* and *von der Weth* considered that recanalisation of the solid choledochus was not effected after the stage of the physiological epithelial occlusion.

In the intestinal tube, it is generally appreciated that epithelial occlu-

sion takes place physiologically in about the second foetal month (*Fischel*), and *Tandler*, *Forssner* and others expounded plausibly the aetiology of congenital intestinal obliteration by means of the supposed failure of the loosening of this occlusion (cited from *Böhm*). That it is not yet settled whether this process occurs physiologically in the primitive choledochus or not, is due largely, I suppose, to the fact that many suitable specimens can not easily be obtained. Yet it seems to me very reasonable to presume that the process happens in the primitive choledochus, because the latter is formed through the narrowing of the hollow hepatic outpouch.

As mentioned above, I have pointed out two conditions indispensable to the development of idiopathic cystic dilatation of the common bile-duct and have interpreted the pathogeny of the disease by preferring two congenital malformations which satisfy the conditions. Next I will attempt to explain the development of these congenital malformations, consulting various possible theories as to the aetiology of both diseases, namely idiopathic cystic dilatation and congenital atresia of the biliary tract. In my opinion, the aetiology of these congenital malformations lies in the inequality of proliferation of the epithelial cells at the stage when the primitive choledochus is still solid — perhaps, at the stage of the physiological epithelial occlusion. As *Beneke* stated, it shows a certain developmental debility of the distal portion of the primitive choledochus that the duct is formed through narrowing of the hepatic outpouch. If inequality of the epithelial proliferation happens at the stage of the physiological epithelial occlusion in such a way that in the distal portion the physiological developmental debility increases, while in the proximal portion the epithelial cells proliferate in excess, then the solid primitive choledochus becomes formed like a bottle set upside down. When the choledochus comes to be cavitied later, the lumen of its proximal thick portion should be abnormally wide — congenital dilatation —, whereas that of its distal thin portion should be abnormally narrow — congenital stenosis. If the developmental debility of the distal portion is but trifling, the stenosis resulting from it may be slight, but if it is of a high degree, the stenosis may be very severe, and finally the duct can not after all be practically hollowed — congenital atresia. If the excessive epithelial proliferation in the proximal portion takes place on all sides and in a large extent of the duct, the dilatation may be shaped somewhat ampullarily; if the cells in a limited part of the proximal portion proliferate especially vigorously on all sides of the duct, the dilatation may

be shaped cystically, and the excessive epithelial proliferation on one side of the duct may make a marked diverticular dilatation (*Flechtenmacher*'s case and so on). The inequality of the epithelial proliferation may be lacking in uniformity in each case. For instance, in the case of slight developmental debility in the distal portion and of marked excess of the epithelial proliferation in the proximal, a medium-sized dilatation may exist at birth, yet it may not give rise to clinical symptoms for a long while, because the stenosis is not severe. On the contrary, in the case of marked developmental debility in the distal portion, the congenital dilatation may be enlarged rapidly owing to the severe stenosis and may cause certain clinical symptoms very early. If the epithelial proliferation declines in a large extent of the choledochus, then congenital atresia of the biliary tract may have happened.

Thus according to my hypothesis, the development of two different congenital malformations which satisfy the two conditions mentioned repeatedly is easily comprehended at once, and my hypothesis also can be applied in order to explain anatomical findings observed in all the cases of both diseases, idiopathic cystic dilatation of the common bile-duct on the one side and congenital atresia of the biliary tract on the other.

Sex and Period of Teratogenetic Termination

It is often said that idiopathic cystic dilatation of the common bile-duct occurs predominantly in females, but in Japan opposite views have been now and then proposed (*Okuya*, *Kadikawa*). In my statistical studies, the ratio of the female comes to 65% in Japanese cases, to 83% in foreign cases and to 76% in the total (Table III), therefore I can not but recognize a certain preponderance of that sex. *Schloessmann* attributed this preponderance to the fact that the congenital malformations were in general of greater frequency in females, but *Seeliger* dissented from this opinion in quoting the fact that the double monsters occurred more frequently in females (*Schwalbe*), but the simple monsters rather more frequently in males (*Marchand*). *Wagner*, *Okuya* and others regarded this to be a mere fortuitous matter.

In the foetal life, the indifferent generative gland turns into a male one at the 13 mm stage and into a female one between the 18 and 20 mm stage (*Fischel*), therefore morphological sexual distinction appears about at the 13 mm stage. On the other hand, the physiological epithelial occlusion of the primitive choledochus is ordinarily seen about at the 7 mm stage

(according to *Hanser* in a 6.75 mm embryo and to *Pfuhl* in a 7 mm), and hence the period of teratogenetic termination (*Schwalbe*) of idiopathic cystic dilatation of the common bile-duct should be, according to my hypothesis, at about the 7 mm stage when no morphological sexual distinction appears. But the period of the epithelial occlusion seems not to be strictly limited as mentioned above. For instance, a photomicrograph of a 7 mm embryo with a hollowed primitive choledochus is given in *Fischel*'s text-book, and on the contrary *Lewis* stated that the solid choledochus began to be cavitied at the 7.5 mm stage and had a lumen completely formed only at the 16 mm stage (cited from *Böhm*). Furthermore *Hanser* said that the developmental periods of the gall-bladder and the extrahepatic biliary tracts were markedly variable in individual cases, and accordingly it was difficult to decide the period of teratogenetic termination of certain congenital malformations in these organs. Therefore, if it can be accepted that the epithelial occlusion continues up to the stage of the sexual distinction, it may be assumed that at that stage the epithelial cells are influenced in some way, especially in females, to cause inequality of their proliferation. Thus, I may say, we can somewhat clarify the obscure predominancy of the female sex.

Abnormalities of the Pancreatic Ducts

Only rarely has the pancreatic duct been particularly examined in cases of idiopathic cystic dilatation of the common bile-duct, yet its abnormalities are pretty frequently given in the literature. Among them, the abnormal length of the ductus pancreaticobiliosus was most commonly encountered (*Arnolds; Kodumi & Kodama; Budde, Sato, T., Fukuda*'s Cases 1 and 2, *Fukamati, Feyrter*, author's Case 1), and for instance this duct was 4.5 cm in length in *Budde*'s case. This abnormality seems to have partially resulted secondarily from the enlargement of the cyst, yet it may be regarded partially as a congenital malformation. And the development of this malformation can be easily understood according to my hypothesis. As is known to all, the pancreas develops from three outgrowths, one dorsal and two ventral or lateral. The left-sided bud soon becomes suppressed, and only the right-sided bud grows further. This bud adheres, on one side, to the primitive choledochus, and its excretory duct combines with the latter; on the other side, it reaches to the dorsal bud, and its excretory duct anastomoses with the middle portion of the duct in that bud. Thus *Wirsung*'s

duct is formed. If the distal portion of the primitive choledochus is formed abnormally narrowly due to abnormal developmental debility, the excretory duct of the right-sided bud can not perform normal anastomosis with it, and thus teratological anastomosis is brought about.

No such complicated abnormalities of the pancreatic ducts as are formed in my two cases are described in the literature on this subject. Perhaps, it is owing to the fact that the ducts were in general not examined closely. The abnormal small duct in Case 2 is nothing but the excretory duct of the right-sided bud the former of which has failed to combine with the duct of the dorsal bud. The development of the abnormal duct in Case 1 can not be easily interpreted, and perhaps, it is based on more serious developmental errors. To my mind, these malformations are also related somewhat to the supposed developmental failure of the primitive choledochus. Hence the pancreatic duct should be more closely examined in future in case of idiopathic cystic dilatation of the common bile-duct.

Occasional Causes

In case of severe congenital stenosis of the distal portion of the common bile-duct, the biliary outflow is hindered without any additional disturbances, and the disease — idiopathic cystic dilatation of the common bile-duct — declares itself very early, but in the case of slight stenosis, occasional causes come to be of greater importance in bringing about clinical symptoms. These occasional causes are such catarrhalic swelling of the mucous membrane of the duct, spasmodic contraction of *Oddi*'s sphincter, foods, pregnancy, etc. as are repeatedly related by many authors.

Among them, pregnancy is most important. In not a few cases of the disease, its first signs burst out or its clinical symptoms became markedly worse during pregnancy or in the puerperal period (*Goldammer, Kremer, Zimmer, McWhorter, Kulakoff, Lange, Erdely*'s Case 2, *Zinninger & Cash*; *Backer-Grøndahl*'s Case 2, *Tailhefer*'s Case 2; *Nakamura, Igarasi & Fukusima*). This fact is also clearly illustrated in Chart I, a graphical representation of Table II, i. e., the female curve rises suddenly between 20 and 25 years to form a very steep mountain whose summit is at 24%, while the male rises but slightly. We can not but consider this marked sexual difference as being caused by the first pregnancy in females at that age. *Goldammer, Kremer, Zimmer* and others thought that the impregnated uterus pressed the intraabdominal organs and in this way caused indirectly

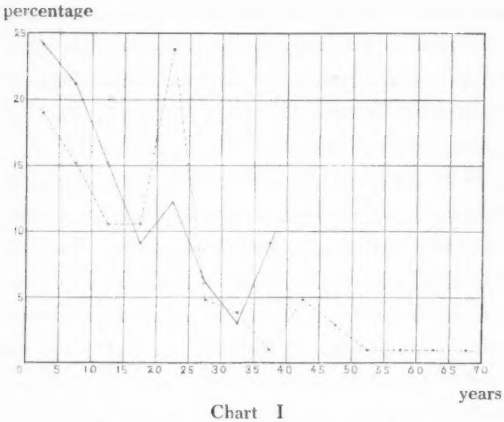


Chart I
Graphic Representation of Table II.
Solid line: male. Broken line: female.

the biliary stagnation. But in several cases (*Erdély*; *Zinninger & Cash*; *Nakamura*, *Igarasi & Fukusima*), the clinical symptoms burst out for the first time or became severer in the second month of the pregnancy. Therefore that explanation can not be applied in such cases. In my opinion, qualitative and quantitative changes of bile due to hypercholesterinaemia, hyperkinetic neurosis of *Oddi*'s sphincter as is supposed by *Westphal* and *Torinoumi* (cited from *Hanser*), etc. during the pregnancy may act greatly in giving rise to the biliary stagnation.

Enlargement of the Cyst

Due to irritation of stagnated bile in the cyst, an inflammatory process may take place in the narrowed distal portion of the common bile-duct, and the connective tissue may proliferate there, as *Ogata* proved. Then the slight stenosis of the distal portion becomes severer, and at last the duct is obliterated (*Buzik*). Presumption of such a pathological process is not only testified to in the actual — in case of congenital atresia of the biliary tract, inflammation of an unknown nature and proliferation of the connective tissue were often observed in the obliterated part, for instance in *Feyrter*'s Case 2—, but also answers for the explanation of cases with atresia of the distal portion of which the former seems irrational at first sight, as follows: — 1. cases with discharge of the meconium — it is said that the biliary secretion begins in the third foetal month (*Hertwig*), and hence in such cases the obliteration must have occurred secondarily after that month —, 2. cases with discharge of the yellow-coloured stool for a certain period after birth, and 3. cases that lived for many years.

As stated in "Comments", the direction of the enlargement of the cyst and that of the distal portion of the common bile-duct cross each other

in proportion as the cyst enlarges. Resulting from this crossing and also from the enlarging of the cyst downwards, a kinking of the distal portion and a valvular infolding at the orifice of the latter may be brought about. If so, they must bear a certain regularity in reference to their situation, i. e., the fold is formed on the opposite side of the turning of the kinking. For this reason, we may decide in some cases whether the kinking is congenital in origin or not.

According to *Rostowzew*'s explanation by means of schematized figures, in case of very severe biliary stagnation due to a valvular fold formed at the orifice of the distal portion, the cyst wall comes to be extended severely, and the infolding becomes scraped off. Then bile flows into the duodenum, and the internal pressure of the cyst diminishes. If the pressure decreases moderately, the infolding reappears, and bile stagnates again. This hypothesis is accepted by most authors, because it is a very reasonable way to explain the variability of the clinical symptoms. It is self-evident that the distal portion ought to be shortened and widened in order to enable the mechanism related by *Rostowzew* to be carried out. But the distal portion used to be in general several centi-meters in length and to be almost always narrowed in the cases of idiopathic cystic dilatation of the common bile-duct. Therefore I consider that that mechanism does not actually take place. To my mind, the variability of the clinical symptoms depends greatly upon the nature of some occasional causes.

If a kinking is once formed in the distal portion of the common bile-duct, it obstructs the biliary outflow and makes the cyst enlarge. On the other hand, it becomes more and more sharpened due to the cystic enlargement, and the lumen of the duct becomes strongly flattened in the neighbourhood of its sharp turning. In that case it may happen that the duct comes to be obliterated secondarily owing to fibrous adhesion of its internal surface.

Conclusions

1. Most of the various aetiological theories referring to idiopathic cystic dilatation of the common bile-duct can be denied logically. Even a few plausible ones are not suitable in explanation of all the anatomical findings observed in the cases of this disease.

2. Certain common features are testified to in the cases of the disease, and hence we can not but consider that the disease is due to some simpli-

fied cause.

3. The disease is caused by certain congenital malformations.

4. As to the pathogeny of the disease, two conditions are demanded. The first is the factor which enables the limited part of the common bile-duct to dilate cystically, and the second is that which makes a pathological state develop into one disease. Of course, the factors satisfying these conditions ought to be congenital in origin.

5. Not only logically, but also actually, the factor which satisfies the first condition is nothing but congenital dilatation of the proximal portion of the common bile-duct, and that which satisfies the second condition is congenital stenosis or atresia of the distal portion.

6. The pathogeny of idiopathic cystic dilatation of the common bile-duct is as follows. In the choledochus with these two congenital malformations, bile stagnates owing to the congenital stenosis or atresia of the distal portion and, in some cases, to certain occasional causes, and the congenital dilatation of the proximal portion enlarges more and more to form at last a large cyst and to cause certain clinical symptoms.

7. The stenosis or atresia of the distal portion is observed almost constantly in the case of idiopathic cystic dilatation of the common bile-duct, and besides, many transitional forms are encountered between the two diseases classified clinically, namely idiopathic cystic dilatation and congenital atresia of the biliary tract. Therefore they are related intimately to each other, are essentially the same from a pathological-anatomical point of view and accordingly should result from the same cause.

8. The legitimate aetiological theory of idiopathic cystic dilatation of the common bile-duct should be able to explain not merely the development of the two congenital malformations stated in Clause 5, but also the aetiology of congenital atresia of the biliary tract.

9. The process named epithelial occlusion seems to take place physiologically in the course of the development of the common bile-duct.

10. To my mind, the causal genesis of idiopathic cystic dilatation of the common bile-duct lies in supposed inequality of epithelial proliferation at the stage of the physiological epithelial occlusion. Since certain developmental debility of the distal portion is in general accepted in the formation of the primitive choledochus, such presumption is not a mere absurd hypothesis.

11. The inequality happens in such a way that in the distal portion

the physiological developmental debility increases in its degree, while in the proximal portion the epithelial cells proliferate in excess. Then the solid primitive choledochus comes to be formed like a bottle set upside down. If cavitied later, it ought to present dilatation in its proximal portion and stenosis in its distal.

12. According to my hypothesis, the development of the two different congenital malformations related in Clause 5 is easily comprehended at once, and moreover, the aetiology of congenital atresia of the biliary tract can be explained.

13. Atresia of the distal portion of the common bile-duct of which the former seems irrational at first sight is easily understood according to my hypothesis and also to the fact that the narrowed distal portion comes to be obliterated secondarily due to proliferation of the connective tissue irritated by stagnated bile.

14. Idiopathic cystic dilatation of the common bile-duct is pretty frequently accompanied by congenital abnormalities of the pancreatic duct. Possibly, they are related somewhat to the supposed developmental error of the primitive choledochus, and hence the pancreatic duct should be, in future, more closely examined in cases of this disease.

15. A kinking of the distal choledochus and a valvular infolding at the orifice of the latter at the inside of the cyst may be formed secondarily in proportion to cystic enlargement. If so, they must bear a certain regularity in reference to their situation. Remembering this, we can decide in some cases whether the kinking is congenital in origin or not.

16. *Rostowzew*'s hypothesis which is accepted by many authors in order to explain the variability of the clinical symptoms is nothing but a mere academic discussion. Actually the variability depends greatly upon the nature of some occasional causes.

17. Among many occasional causes pointed out by authors, pregnancy is most important. During it, not only does the impregnated uterus obstruct the biliary outflow mechanically, but also the qualitative and quantitative changes of bile, the hyperkinetic neurosis of *Oddi*'s sphincter, etc. may have a great part in giving rise to the biliary stagnation.

18. Idiopathic cystic dilatation of the common bile-duct occurs predominantly in females, yet it is very difficult to discover the final cause of that.

19. The reported cases are a boy 2 and a half years of age and a

Table

No.	Author	Year	Age	Sex	Beginning of the disease	Cardinal symptoms	Diagnosis	Operation	Progress	Cyst		
										Size	Shape	Contents
1	*Sakuma*	1905	1 yr. & 9 mos.	f.	5 mos. previously; jaundice, purpura, acholia	Jaundice, haemorrhagic diathesis, acholia, emaciation, abdominal swelling, a globular tumour of the size of a fist	Hepatic sarcoma?	Not performed	Death; autopsy	Of the size of a child's head	Globular	650 cc; dark red, turbid fluid
2	*Niizawa (Nagao, Case 12)*	1906	3 yrs. & 1 mo.	m.	2 mos. & a half previously; jaundice, abdominal tumour	Jaundice, emaciation; a large, elliptical tumour	Dilatation of the gall-bladder	2 times; cholecdochoduodenostomy, gastroenterostomy	Death on the following day of the 2nd operation; autopsy	Of the size of a man's fist (at autopsy)	Elliptical	800 cc; green bile (at operation)
3	*Kaira*	1907	2 yrs. & 8 mos.	m	1 yr. previously; abdominal tumour	Jaundice, abdominal tumour		Not performed	Death; autopsy	14:12:5.5 cm, of the size of a child's head		500 cc; bile
4	*Mayesima*	1912	2 yrs. & 2 mos.	m.	1 yr. previously; abdominal swelling	Jaundice, emaciation, ascites, abdominal swelling, a tumour of the size of an adult's head	Retroperitoneal cyst	Aspiration	Death 2 mos. after the operation; autopsy	15:12 cm, of the size of a child's head		Yellowish-green, stinking, turbid fluid
5	*Sekiguti*	1912-13	25 yrs.	f.	2 yrs. previously; pain like colic due to gall-stones, jaundice	Colic, jaundice, abdominal swelling, a tumour of the size of the palm of a hand	Cholelithiasis	Resection of the cyst	Death on the very day of the operation; autopsy	Of the size of a child's head		600 cc; serо-mucous fluid
6	*Suda*	1912-13	6 yrs.				Dilatation of the gall-bladder	2 times; cholecdochogastrostomy, gastroenterostomy				
7	*Kuru*	1913	7 yrs.	f.	4 yrs. previously; right upper abdominal pain	Jaundice, acholia, emaciation, attacks of abdominal pain, abdominal swelling, a tumour of the size of a child's head		2 times; resection of the cyst, cholecystoenterostomy	Death 20 days after the 2nd operation; no autopsy	15:13:10 cm, of the size of a child's head	Elliptical	1200 cc; green, slightly turbid fluid
8	*Kodumi & Kodama*	1916	15 yrs.	f.	1 yr. previously; resistance in the right hypochondrium	Jaundice, itching, haemorrhagic diathesis, eosinophilia, a tumour of the size of the palm of a hand	Echinococcus of the liver?	Not performed	Death; autopsy	36 cm in circumference, of the size of a child's head	Globular	700 cc; deep green, not mucous bile
9	*Sugeya*	1918	17 yrs.	f.	10 yrs. previously; attacks of abdominal pain	Jaundice, vomiting, loss of appetite, abdominal swelling, attacks of abdominal pain, pain on pressure and resistance in the right hypochondrium	Obliteration of the biliary tract and cholaemia	Not performed	Death; autopsy	15.5:10 cm, of the size of a child's head		700 cc; bilious fluid
10	*Hayasi*	1920	1 yr. & 4 mos.	f	6 mos. previously; abdominal swelling	Vomiting, ascites, abdominal swelling	Cyst	Not performed	Death; autopsy	Of the size of a child's head		1500 cc; dark brownish-green, slightly turbid fluid
11	*Ito*	1920	11 yrs.	m.	2 mos. previously; abdominal pain	Jaundice, acholia, vomiting, abdominal pain, a cystic tumour of the size of a child's head	Pancreatic cyst or dilatation of the common bile-duct?	Insertion of an elastic drainage-tube between the cyst and the duodenum	Death 1 wk after the operation, no autopsy	Larger than a child's head		1400 cc, transparent, bilious fluid
12	*Yasui*	1920	1 yr. & 4 mos.	f.	5 mos. previously; abdominal swelling	Intermittent jaundice, abdominal swelling, a tumour of the size of a child's head		Choledochocho-denostomy	Death on the 5th day after the operation; autopsy	9:8:8 cm (at autopsy); of the size of a child's head (at operation)	Globular	950 cc, dark green fluid (at operation)
13	*Sato, T*	1920-21	37 yrs.	m.	6 yrs. previously; vomiting, diarrhoea	Nausea, vomiting, emaciation, constipation, slight abdominal pain, a hard tumour of the size of a hen's egg	Gastric carcinoma	3 times; fixation of the cyst on the abdominal wall, aspiration, gastroenterostomy	Death on the 4th day after the 3rd operation; autopsy	Of the size of a child's head		More than 600 cc; greenish-brown, stinking, mucous fluid
14	*Yamanouti, Case 1*	1921-22	4 yrs.	f.		Attacks of severe abdominal pain, jaundice, a tumour of the size of a child's head		Aspiration				
15	*Yamanouti, Case 2*	1921-22	16 yrs.	f.	High fever	High fever, diarrhoea, vomiting, abdominal tumour		Aspiration				
16	*Fukuda, Case 1 Itoi, 1921-22)*	1922	19 yrs	m.	Since boyhood; attacks of slight sting in the right hypochondrium	Jaundice, steatorrhoea, attacks of sting, upper abdominal swelling, a fluctuating tumour with pain on pressure	Cyst of the liver or of the pancreas?	Biliary fistula	Death on the 4th day after the operation; autopsy			More than 5000 cc; yellowish-green, dilute, bilious fluid (on exploratory puncture)
17	*Fukuda, Case 2*	1922	2 yrs.	f.	5 mos. previously; abdominal swelling	Jaundice, intermittent acholia, diarrhoea, abdominal swelling, a fluctuating tumour		Choledocho-duodenostomy	Death on the 25th day after the operation; autopsy	Of the size of an adult's fist		200 cc, yellowish-green, dilute, bilious fluid
18	*Kawasi*	1922-23	4 mos.	f	Since birth; abdominal swelling	Intermittent jaundice, abdominal swelling, a large tumour	Tumour of the kidney	Choledocho-duodenostomy	Death on the very day of the operation; autopsy			500 cc; deep green fluid
19	*Idumi*	1923	13 yrs	f.	5 mos. previously; chill, fever, colic, vomiting, jaundice, right upper abdominal tumour	Jaundice, colic, loss of appetite, emaciation, a tumour of the size of a child's head	Obliteration of the common bile-duct due to gall-stones and dilatation of the gall-bladder	Choledocho duodenostomy	Recovery	Of the size of a child's head		2700 cc, yellowish-blue, turbid fluid
20	*Narabayasi*	1923	2 yrs. & 9 mos.	m	Since infancy at the breast; right upper abdominal swelling	Jaundice, acholia, epistaxis, emaciation, chill, fever, a tumour of the size of a child's head	Obliteration or cyst of the common bile-duct	Choledocho-duodenostomy	Recovery	Of the size of a child's head		1300 cc; light green, slightly mucous bile
21	*Tanaka*	1924	7 yrs. & a half		Ca. 1 yr. previously; jaundice, haemorrhagic diathesis	Jaundice, haemorrhagic diathesis, abdominal swelling, a globular, fluctuating tumour of the size of a child's head		Performed	Death 1 wk after the operation			
22	*Fukamati*	1925	14 yrs	f	1 yr. & a half previously; jaundice	Jaundice, ascites, a tumour of the size of a man's head	Hepatic carcinoma?	Not performed	Death; autopsy	22 cm in length		2700 cc; bile
23	*Kawasa*	1925	8 yrs	f.								1200 cc
24	*Sato, M.*	1926	12 yrs.	f	3 mos. previously; chill, fever, pain in the hepatic region	Jaundice, diarrhoea, fever, pain, abdominal swelling, a tumour of the size of a man's fist	Abscess of the liver?	Biliary fistula	Death on the very day of the operation; autopsy	Of the size of double fists		500 cc, green, transparent fluid
25	*Akiya, Case 1*	1926-27	10 yrs	m	6 mos previously; right upper abdominal tumour	Jaundice, haemorrhagic diathesis, vomiting, fever, a right upper abdominal tumour		Evacuation	Death autopsy	Large		
26	*Akiya, Case 2*	1926-27	35 yrs	m.	3 mos. previously; dysgnoea, vomiting, right upper abdominal tumour	Jaundice, dyspnoea, a tumour of the size of an adult's head		Performed	Death on the following day of the operation, autopsy			
27	*Kawasa*	1926-27	7 yrs.	f		Slight jaundice, vomiting		Biliary fistula				

I. A

Stones	Constituents	Hepatic duct	Cystic duct	Gall-bladder	Distal portion of the common bile-duct		Pancreatic duct	Duodenal papilla	Liver	Notes
					Orifice	Course				
	Common bile-duct, cystic and common hepatic ducts	Severely dilated	Of the size of a red bean	Contains reddish brown, dilute fluid, its wall thickened	Narrowed, 1–2 mm in diameter, a probe introduced enters the duodenum			Passable for a probe to an extent of 1 cm	Biliary cirrhosis	
				Collapsed, contains a small quantity of bile	Can not be seen	Can not be seen	Opens to *Santorini's* papilla	*Vater's* papilla can not be seen	Biliary cirrhosis	On exploratory puncture green bile drawn out
	Common bile-duct, cystic and common hepatic ducts	Dilated, of the size of a finger	Not dilated	Collapsed	Severely narrowed	Kinked			Biliary cirrhosis	
	Common bile-duct, cystic, common hepatic and pancreatic ducts			Normal-sized	Passable for a probe	2 cm in length, slightly kinked	Opens to the cyst at the point 3 cm apart from the orifice of the distal portion		Biliary cirrhosis	
				Severely collapsed	Moderately narrowed					
						Can not be seen				
	Common bile duct				3 cm in diameter, round					Diverticular dilatation of one side of the common bile-duct
	Common bile-duct, cystic and both hepatic ducts	Of the size of a little finger	5 cm in length, of the size of a little finger		Severely narrowed; valvular infolding at the inferior margin	2.5 cm in length, kinked	Combines right-angularly with the distal portion; ductus pancreaticobilious 3 cm in length	A probe introduced does not enter the cyst	Biliary cirrhosis	
		Dilated, 2.5 cm in diameter	Dilated, 1.5 cm in diameter			Obliterated at the point 2 cm distant from *Vater's* papilla		Passable for a probe	Swollen	
	Common bile-duct	Dilated, of the size of a thumb			Can not be seen	Can not be seen	Not dilated	Can not be seen	Slight increase of connective tissue in *Glisson's* capsules	
	Common bile-duct, cystic and common hepatic ducts?			Normal-sized, filled up	Can not be seen				Swollen	Ascites (at operation)
	Common bile-duct, cystic and common hepatic ducts	Dilated; the left hepatic duct 0.8 cm in width, the right 1 cm	0.5 cm in width, 2 cm in length	Collapsed	Very small; sickle-shaped fold at the upper margin	Ramifies into 2 narrow ducts, both of them passable only for a bougie and kinked; one 2.5 cm in length opens to *Vater's* papilla, the other 1 cm in length combines with the pancreatic duct	3 mm in width; opens to *Santorini's* papilla which lies 2 cm apart from *Vater's* papilla; combines with one branch of the distal portion at the point 1 cm distant from the duodenal opening		Initial biliary cirrhosis	On exploratory puncture 800 cc of dark green fluid drawn out
Several dozens of polygonal, white stones of the size of a rice-grain	Common bile-duct, cystic and both hepatic ducts	Passable for a probe	Obliterated	Severely collapsed, contains a small quantity of mucous bile and numerous white stones of the size of a rice-grain	Narrowed, passable for a probe	2 cm in length	Not dilated; ductus pancreaticobilious 1.5 cm in length		Slight increase of connective tissue around the small biliary ducts	
	Common bile-duct, cystic and common hepatic ducts		Flattened, kinked	Collapsed, contains no bile; its wall thickened	Narrowed, passable for a probe	1.5 cm in length, severely kinked	Combines right-angularly with the distal portion; ductus pancreaticobilious 1 cm in length		Biliary cirrhosis	On exploratory puncture 5000 cc of yellowish-brown fluid drawn out; suppurative peritonitis
	Common bile-duct, cystic and common hepatic ducts	Not dilated		Contains but a small quantity of dilute bile			Ramifies into 2 ducts; one of them 2.8 cm in length, thicker than the other, opens to *Santorini's* papilla; the other 3.2 cm in length combines immediately with the cyst and then opens to *Vater's* papilla; ductus pancreaticobilious 2.5 cm in length		Fatty degeneration and jaundice	
				Normal-sized		Can be seen			No remarkable pathological changes	
			Embedded in cicatrical tissue	Collapsed, its wall thickened	Passable for a probe to an extent of ca 1.5 cm					
				Collapsed					Slightly swollen	
										Exploratory puncture
	Common bile-duct, cystic and common hepatic ducts?		6 cm in length of the size of a little finger	Contains one and a half spoonful of bile	Passable for a probe	5 cm in length	Ductus pancreaticobilious 2 cm in length	Passable for a probe	Biliary cirrhosis	
	Common bile-duct, cystic and common hepatic ducts	Dilated, passable for a finger	Dilated, of the size of a hen's egg; kinked	Slightly enlarged, 5×3.5 cm	Narrowed; infolding at the margin	Ca 1 cm in length	Ductus pancreaticobilious very short		Initial biliary cirrhosis	Ascites (at autopsy)

Table

No.	Author	Year	Age	Sex	Beginning of the disease	Cardinal symptoms	Diagnosis	Operation	Progress	Cyst		
										Size	Shape	Contents
28	*Motoki*	1926-27	8 yrs.	m	Half a mo. previously; fever, nausea, vomiting, abdominal pain, a tumour with pain on pressure in the right hypochondrium	Emaciation, abdominal pain, a fluctuating tumour of the size of a child's head		Biliary fistula	Good			Bilious fluid
29	*Kawasaki*	1927	3 yrs.	f	11 mos. previously; abdominal swelling	Jaundice, haemorrhagic diathesis, emaciation, abdominal swelling, resistance in the ileocecal region, gall-bladder palpable		Not performed	Death; autopsy	Larger than an egg of ostrich		Haemorrhagic, bilious fluid
30	*Tadenuma*	1927	29 yrs.	m	Since infancy; severe pain on pressure in the right hypochondrium	Slight jaundice, emaciation, pain and colic in the right hypochondrium, a fluctuating tumour of the size of the palm of a hand	Cholelithiasis	4 times; biliary fistula, choledochojejunostomy	Recovery	Of the size of a man's head		1000 cc., slightly turbid, bilious fluid
31	*Kato, R. (Kato, R. & Iimura, S.)*	1928	25 yrs.	m	3 mos. previously; attacks of pain in the right upper abdomen	Jaundice, attacks of pain, abdominal swelling, a tumour of the size of a man's head, gall-bladder palpable	Pancreatic cyst and obliteration of the common bile-duct	Choledochoduodenostomy	Recovery	Of the size of a man's head		4000 cc.; aseptic, light brown, serous fluid mingled with mucous substances
32	*Okuya, Case 1*	1928	10 yrs.	m	7-8 mos. previously; abdominal swelling	Jaundice, haemorrhagic diathesis, acholia, vomiting, emaciation, lumbago, abdominal swelling, a slightly fluctuating tumour of the size of a man's head	Cystic dilatation of the common bile-duct	Fixation of the cyst on the abdominal wall	Death on the 9th day after the operation; autopsy	21:16 cm	Elliptical	1700 cc., aseptic, bilious fluid
33	*Okuya, Case 2*	1929	36 yrs.	m	3 mos. previously; sense of oppression of the chest, vomiting, slight jaundice, a right upper abdominal tumour of the size of a goose egg	Intermittent jaundice, colic, vomiting, loss of appetite, emaciation, a globular tumour of the size of a child's head		Fixation of the cyst on the abdominal wall	Death 20 hrs. after the operation; autopsy	20:18:8 cm, of the size of a man's head	Elliptical	Dark green bile
34	*Watanabe*	1928-29	21 yrs.	m			Abdominal tumour	2 times; biliary fistula, choledochoduodenostomy	Death; autopsy			
35	*Kato, K.*	1928-30	8 yrs. & a half	f	1 yr. & a half previously; abdominal pain	Vomiting, loss of appetite, abdominal pain and swelling, a tumour larger than a fist	Intestinal invagination?	Biliary fistula	Death on the 4th day after the operation; autopsy	12:7.5 cm, larger than an adult's fist	Peach-shaped	350 cc.; blackish-green, slightly thickened, bilious fluid
36	*Isawa*	1929-30	25 yrs.	f	2 mos. previously; sense of tension in the upper abdomen, chill, fever	Sense of tension in the upper abdomen; a globular, fluctuating tumour of the size of a child's head	Hydronephrosis or echinococcus of the liver?	Choledochoduodenostomy	Recovery	Large		1100 cc.; light green, stinking, turbid fluid
37	*Kadokawa*	1930	1 yr. & a half	f	2 mos. previously; vomiting, fever, constipation	Vomiting, constipation, a smooth tumour	Dilatation of the common bile-duct	Choledochoduodenostomy	Recovery	Of the size of a goose egg		Transparent bile
38	*Kambe*	1930	21 yrs.	f	1 yr. & a half previously; jaundice	Intermittent jaundice, dull pain in the hypochrium, a semi-globular tumour of the size of an adult's fist		Choledochojejunostomy	Recovery	Of the size of a child's head	Semi-globular	800 cc.; aseptic, black bile mingled with sandy substances
39	*Terada & Yase (Yase, 1928)*	1930	4 mos. & a half	m	Since the 2nd postnatal wk.; jaundice	Jaundice, haemorrhagic diathesis, acholia, vomiting, a tumour of the size of an adult's fist		Not performed	Death; autopsy	10:8:5 cm	Elliptical	120 cc.; dark brown, coffee-like, dilute fluid
40	*Iimura, Case 1*	1930-31	54 yrs.	f		Attacks of pain in the hypochondrium	Cholecystitis	Performed				
41	*Iimura, Case 2*	1930-31	44 yrs.	f		Attacks of pain in the hypochondrium	Cholecystitis	Performed				
42	*Iimura, Case 3*	1930-31	17 yrs.	f		Attacks of pain in the hypochondrium	Cholecystitis	Performed				
43	*Kuriyama*	1931	4 mos.	f	3 mos. previously; jaundice, abdominal swelling	Jaundice, acholia, emaciation, abdominal swelling, a large, fluctuating tumour	Congenital cyst of the common bile-duct	Not performed	Death; autopsy	Of the size of a child's head		
44	*Ogawa*	1931	6 mos.	f	1 mo. previously	Acholia, vomiting, fever, abdominal swelling, a cystic tumour		Not performed	Death; autopsy	11:14:9 cm	Almost globular	1300 cc.; yellowish-green, somewhat purulent fluid
45	*Tanaka, Case 1*	1931	1 yr. & a half	f	2 mos. & a half previously; vomiting	Vomiting, right abdominal swelling, a fluctuating tumour larger than a fist		Choledochoduodenostomy	Recovery	Of the size of a hen's egg		Transparent, bilious fluid
46	*Tanaka, Case 2*	1931	1 yr. & 11 mos.	f	1 wk. previously; vomiting, fever, abdominal pain	Slight jaundice, vomiting, fever, abdominal pain and swelling	Intestinal obliteration?	Performed	Death	Of the size of a hen's egg	Globular	
47	*Ochi*	1931	21 yrs.	f	3 mos. previously; painful swelling in the right hypochondrium	Jaundice, acholia, right upper abdominal swelling, a painful tumour of the size of an adult's head	Cholecystitis, pancreatic cyst or echinococcus?	Biliary fistula	Death on the following day of the operation; autopsy	Of the size of an adult's head	Almost globular	Blackish-green, thickened bile
48	*Kamiya*	1931-32	8 yrs.	f	1 mo. previously; upper abdominal pain, jaundice	Jaundice, vomiting, abdominal pain and swelling, a tumour of the size of a child's head		Choledochogastrostomy, gastroenterostomy, enteroenterostomy	Good	Of the size of a child's head		750 cc.; blackish-yellow bile
49	*Isoda & Kameda*	1932	52 days		Since the 4-5th postnatal day; acholia	Jaundice, haemorrhagic diathesis, acholia, emaciation, abdominal swelling		Not performed	Death; autopsy	Of the size of a goose egg		Thickened, mucous fluid
50	*Akamine*	1932-33	8 mos.	f	2 mos. previously; jaundice	Jaundice, vomiting, upper abdominal swelling, a fluctuating tumour of the size of a child's head		Not performed	Death; autopsy	Of the size of a child's head		Slightly haemorrhagic bile
51	*Kuriyama*	1933-34	6 yrs. & 5 mos.	m	5 mos. previously; jaundice	Jaundice, acholia, emaciation, abdominal pain and swelling, a globular, fluctuating tumour of the size of a child's head	Congenital cyst of the common bile-duct	Choledochoduodenostomy	Death on the 4th day after the operation; autopsy	Of the size of a child's head		1500 cc.; yellowish-brown, transparent fluid
52	*Nakamura (Iwasa, H. & Fukuura)*	1935	22 yrs.	f	2 mos. previously; loss of appetite, nausea, vomiting	Loss of appetite, nausea, vomiting severe right upper abdominal pain, an elliptical tumour of the size of an adult's fist	Cholelithiasis and dilatation of the gall-bladder	Biliary fistula	Death on the following day of the operation; autopsy	9.5:7.0:3.0 cm (at autopsy); of the size of a child's head (at operation)	Elliptical	500 cc.; purulently turbid bile with abundant strepto-cocci and a number of staphylo-cocci and coli-bacilli
53	Author's Case 1	1936	2 yrs. & a half	m	1 mo. & a half previously; tension in the upper abdomen	Vomiting, constipation, oliguria, tension in the upper abdomen, a large, fluctuating tumour	Cyst of the common bile duct	Not performed	Death; autopsy	22.5 cm in length, larger than a child's head	Gourd-shaped	1600 cc.; light green, slightly turbid and mucous fluid
54	Author's Case 2 (*Imai*, 1934)	1936	22 yrs. & 5 mos.	f	1 yr. & a half previously; slight oedema of the eye-lids, jaundice, itching of the skin, faintness, headache, vomiting, a tumour of the size of a hen's egg in the right hypochondrium	Intermittent jaundice and acholia, constipation, loss of appetite, emaciation, abdominal pain and swelling; an elliptical, fluctuating tumour larger than an adult's head	Cyst of the common bile duct	Choledochoduodenostomy, cholecystectomy	Death on the following day of the operation; autopsy	23:18 cm (at autopsy; larger than an adult's head (at operation)	Elliptical	5200 cc.; dark green, faecally stinking fluid with abundant strepto-cocci and coli-bacilli (at operation)

I, B

Stones	Constituents	Hepatic duct	Cystic duct	Gall-bladder	Distal portion of the common bile-duct		Pancreatic duct	Duodenal papilla	Liver	Notes
					Orifice	Course				
										On exploratory puncture bilious fluid drawn out
	Common bile-duct, cystic and common hepatic ducts			Filled up	Moderately narrowed, passable for a probe	2 cm in length; severely kinked at its middle portion		Passable for a probe	Biliary cirrhosis	Ascites (at autopsy)
–					Not stenosed					
–	Common bile-duct, cystic and both hepatic ducts?	Passable for 3 fingers	Dilated	Of the size of a hen's egg	Not passable for a probe; sickle-shaped fold at the margin					
–	Common bile-duct, cystic and both hepatic ducts	Dilated	Dilated		Can not be seen	Can not be seen	Opens to *Vater's* papilla	A probe introduced does not enter the cyst	Severe biliary cirrhosis	
	Common bile-duct, cystic and common hepatic ducts	Dilated, of the size of a fore-finger			Passable for a probe	Not kinked, opens to *Vater's* papilla				Ascites (at operation)
–	Common bile-duct, cystic and common hepatic ducts	Moderately dilated	Moderately dilated	Normal-sized	Passable for a probe					
–				Collapsed	Barely passable for a probe	Not kinked				
				Normal-sized, filled up						
–	Common bile-duct, cystic and common hepatic ducts?			Collapsed, 2 cm in length	Dented, not passable for a probe					1 yr. previously miscarriage, thereafter jaundice and fever for a week
–	Common bile-duct, cystic and common hepatic ducts	Dilated	Dilated	Dilated, contains dark brown, mucous bile	Sickle-shaped fold at the anterior margin	Ca. 1 cm in length, kinked right-angularly; distal 0.6 cm severely narrowed and passable only for a hair		A probe introduced does not enter the cyst	Biliary cirrhosis	
										In 2 cases, a probe introduced in the orifice of the distal portion enters the duodenum; cholecystectomy performed with good results in 2 cases
						Can not be seen		Not passable for a probe	Biliary cirrhosis	Death of pneumonia
	Common bile-duct, cystic and both hepatic ducts?									On exploratory puncture dark green fluid drawn out; suppurative cholecystitis, cholangitis and pericholangitis
				Filled up; opens immediately to the cyst						
										Biliary peritonitis
	Common bile-duct, cystic and both hepatic ducts	The left hepatic duct passable for 2 fingers, the right for 4		Slightly dilated; its neck almost of the size of a pencil opens immediately to the cyst	Valvular infolding	Of the size of the head of a pencil; kinked		Fibrosed; passable only for a hair		
										On exploratory puncture 500 cc of bilious fluid drawn out
						Obliterated		Passable only for a hair, and that to a small extent		
	Common bile-duct, cystic and common hepatic ducts		Obliterated	Collapsed		Obliterated		Clearly visible	Biliary cirrhosis	Ascites (at autopsy)
									Shows recent pathological changes	Peritonitis
–		Not dilated	Dilated, of the size of a thumb	Normal-sized	Narrowed, passable for a probe					The first signs of the disease burst out in the 2nd month of the pregnancy; thereafter artificial miscarriage
–	Common bile-duct, cystic and common hepatic ducts	Passable for a pencil	Dilated, passable for a little finger	Dilated, 10 cm in length	Narrowed, of the size of a bougie; valvular infolding at the left posterior margin	0.8 cm in length; severely kinked	17 cm in length; ductus pancreaticobiliosus 3.7 cm in length; an abnormal duct from *Santorini's* papilla opens to the ductus pancreaticobiliosus	*Santorini's* papilla blind	Initial biliary cirrhosis, cholangitic abscesses	Exploratory puncture performed 3 times; every time light green, serous fluid drawn out
–	Common bile-duct, cystic and common hepatic ducts	Dilated, of the size of a little finger	Dilated	Slightly dilated, contains but a small quantity of thickened bile (at operation)	Pin-head sized, round	2 cm in length; not kinked	Main pancreatic duct opens to *Santorini's* papilla; an abnormal duct from the uncinate process combines with the distal portion		Initial biliary cirrhosis	Exploratory puncture performed several times; every time ca. 3000 cc of dark green, bilious fluid drawn out

single woman 22 years and 5 months old. The cyst in Case 2 is the largest among 54 Japanese cases. In both cases, stenosis of the distal portion of the common bile-duct and abnormalities in the course of the pancreatic ducts were observed.

Addendum

After I had finished this article, another case of idiopathic cystic dilatation of the common bile-duct came under our observation. Since that case seems us to be very interesting in several points, I will append it here briefly as Case 3.

Case 3: A girl 12 years and 2 months of age; autopsy-number 194, 1935.

Clinical History: A girl 12 years of age was admitted on the 15th of August, 1935, into Prof. *Kato*'s internal clinic of the Tohoku Imperial University under cardinal complaints of jaundice, abdominal swelling and abdominal tension. From 4 years of age, the patient had suffered about two times a year from occasional attacks of epigastrial pain, nausea, vomiting, diarrhoea and slight jaundice, all of which lasted in general about a week. In April 1934, she again had these troubles. They disappeared a week later with the exception of the jaundice, which on the contrary gradually increased. From April 1935, her abdomen began to swell and to tighten, and the abdominal swelling augmented especially rapidly from the beginning of August.

On examination, the skin and bulbular conjunctiva on both sides were found to be severely jaundiced. The face was bloated, and both legs oedematous. The abdomen was greatly swollen, and marked dilatation of subcutaneous veins could be seen there. The abdominal wall felt in general tense and especially hard in the epigastrial and right hypochondrial regions. The liver was enlarged and hard, and its surface smooth. Attached to the anterior margin of the liver, a globular tumour of the size of a goose egg was palpated in the right hypochondrium (dilated gall-bladder). The spleen was also enlarged and could be felt in the left hypochondrium. The urine was clear and seemed brownish, and *Gmelin*'s test of it was strongly positive. The ascites was yellowish and clear, and *Rivalta*'s probe of it was negative. The faeces was somewhat acholic.

During her stay in the hospital, the abdominal circumference increased by degrees, and from the lst of October, another vaguely contoured resistance somewhat larger was felt beneath the liver. The resistance grew larger day by day, and the liver later felt coarse-granular. From the 25th of October, she complained of cardiac weakness, and died on the 31st of the same month under cardiac paralysis.

Clinical Diagnosis: Hepatic tumour and right renal tumour?

Autopsy Findings: The skin in general and also the conjunctiva pale and slightly jaundiced. The abdomen was slightly swollen and fluctuating, and about 720 cc of icteric fluid with fibrinous flocculi gathered in the abdominal cavity.

A cystic mass of the size of a child's head appeared in the right abdomen beneath the liver. The small intestines were pressed by this

tumour to the left and downward, and the transverse colon adhering to the anterior tumour surface lay across the middle part of the latter. The duodenum, also tightly adherent to the tumour surface, descended at first from the left upper margin of the tumour toward the middle portion of the anterior surface, bent at the inferior margin to the left and ran into the ascending part. The pancreas was 15.5 cm in length, and its head and uncinate process adhered to the left half of the anterior tumour surface and also to the adjacent inferior surface, and spread over the latter in a thin layer. The pancreatic tissue seemed quite anaemic, and no marked increase of its interstitium could be observed. The gall-bladder was situated at the right upper margin of the tumour; its fundus was dilated to the size of a small apple, and its neck which was combined with the right upper end of the cystic mass was as thick as a thumb. If the gall-bladder was compressed, its contents flowed easily into the cystic mass. The liver to whose port the tumour was tightly bound to the extent of a small goose egg in size was slightly swollen and firm; its surface was coarse-granular and deep green in colour. At the posterior surface of the right hepatic lobe, a round swelling, which was of the size of an apple and felt quite cystical, came forward at the right side of the so-called hepatic part of the inferior vena cava.

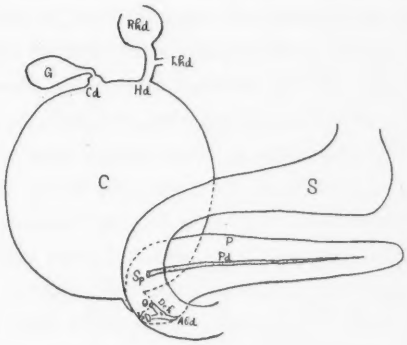


Fig. 3
Schematized Figure of the Cyst of Case 3.
Rhd: cystically dilated right hepatic duct. Lhd: left hepatic duct. Otherwise as in Figs. 1 and 2.

The cystic mass was globular in form, 16 : 16 : 14 cm in diameter and greatly fluctuating. Its surface, completely covered with a serous membrane, seemed anaemic and grayish but glimmered through greenly now and then. There were many dark green flattened lymphatic glands of the size of a cherry stone embedded in the subserous tissue.

When the cyst wall was cut off, the contents of the cyst, together with those of the gall-bladder and of the cyst in the posterior part of the right

hepatic lobe, flowed out at once. They came in all to 2250 cc, were dark brownish-green and slightly mucous and contained no gall-stones. The wall of the gall-bladder was slightly thickened, and its inside was covered with a mucous membrane and seemed anaemic and somewhat greenish. The cyst wall was thin and at most could not be thicker than 0.2 cm. Its inside was in general smooth, anaemic and grayish and showed numerous lentil-sized oval and slightly elevated spots or shallow ulcers covered with blackish-green crustaceous substances.

At the inside, a large opening large enough to let in a thumb comfortably was found at the upper end of the cyst and somewhat to the right. This opening was nothing but the orifice of the dilated common hepatic duct, and its left anterior margin was valvularly sharpened. By inserting a finger into it, it could easily be learned that the left hepatic duct was dilated to the size of a pencil and ramified at a point a few centi-meters distant from the entrance. A finger, introduced into the dilated right hepatic duct, entered immediately into the cyst in the posterior part of the right lobe, showing therefore that the cyst was a globularly dilated portion of the duct. At the right anterior side of this opening and about 4 cm distant from it, another dent with a pencil-sized opening leading to the gall-bladder could be seen (the orifice of the cystic duct). Around these openings, the inside of the cyst wall was especially smooth, lacking in crustaceous substances and seemed as if covered with a mucous membrane.

A hole, larger than a pigeon egg and a few centi-meters in depth, was found at the left lower end of the cyst. At the entrance of this hole, the tissue of the cyst wall was greatly thickened and felt especially firm, i. e., there was formed a margin, and moreover, the left margin was somewhat sharpened off, denoting a former valvular infolding. The anaemic grayish inside of the hole showed several indistinct circular folds arranged in tiers, and besides, a sickle-shaped valvular infolding was seen at the left wall near to the bottom. On close examination, a slit-like opening could be found at the left half of the bottom. Narrowly it let in a thin bougie, which met before long with an invincible hindrance. The cyst wall was especially thinned and partly translucent at the right half of the bottom.

Then the stomach and duodenum were opened. The gastric mucous membrane was anaemic and rich in folds. The duodenum was elongated and widened, and its anaemic mucous membrane was not imbibed with bile. About 8.5 cm distal from the pyloric ring, *Santorini*'s papilla came forth

as a round opening of the size of half a millet-seed. *Vater*'s papilla lay 4.5 cm further distal from *Santorini*'s, was normal in form and was provided with a wide opening. A bougie, inserted in this opening, did not enter the pancreatic body, but it ascended at first a little way along the duodenal wall to bend to the left and downward and to enter the uncinate process which spread over the left inferior cyst surface. This abnormal duct was 5 cm in length, and after it was cut off, it was found to be covered with a mucous membrane. If carefully examined, two small openings of the size of half a millet-seed could be seen at the inside of this duct. They were 2.5 cm distant from *Vater*'s papilla and 0.4 cm apart from each other. A bougie, put into one of them, came out of the other, and that, introduced in the slit-like opening at the left lower end of the cyst, came out of both of them. Hence it was easily understood that they were nothing but junctions between the distal portion of the common bile-duct and the abnormal pancreatic duct. In other words, the distal portion, which was 0.6 cm in length and as thin as a thin bougie, was not kinked and it ramified into two ducts immediately before it combined with the abnormal pancreatic duct. The ductus pancreaticobiliosus measured accordingly 2.5 cm in length and 1 cm in width, and the abnormal duct originating from the uncinate process 2.5 cm in length and 0.5 cm in width. The main pancreatic duct, 13 cm in length, was straightened, passed through the pancreatic head which spread over the cyst surface, and opened into *Santorini*'s papilla.

Post-mortem Diagnosis: Idiopathic cystic dilatation of the common bile-duct. Abnormalities in the course of the pancreatic ducts. Accessory pancreas in the subserous tissue of the small intestine. Cystic dilatation of the right hepatic duct. Dilatation of the gall-bladder. Elongation of the duodenum. Severe biliary cirrhosis of the liver. General jaundice. Recent haemorrhage in the right cerebellular hemisphere. Petechiae at the epicardial surface. Ascites. Cyanotic induration of the spleen. Oedema of both legs, of the lungs and of the mucous membrane of the large intestine. Dilatation of subcutaneous veins of the breast. Swelling of the mesenterial, perigastrial, retroperitoneal and mediastinal lymphatic glands.

Microscopical Findings: The cyst wall consisted of dense fibrous tissue with scanty elastic fibrils. Its inside, in general lacking in ordinary epithelial covering, was often provided with crustaceous substances out of bile-pigment, but now and then a single-layered columnar epithelium could be seen particularly in coincidence with the macroscopical lentil-sized and slightly

elevated spots. Localized infiltrations of polymorphonuclear leucocytes were scattered in the fibrous tissue especially markedly under the crustaceous substances. At the inside of the hole situated at the left lowar end of the cyst, a number of strands of well preserved non-striated muscular fibers were observed near to the basement membrane.

The liver showed typical advanced biliary cirrhosis with a luxuriant new-growth of small biliary ducts. Greater biliary ducts were sometimes dilated, and their epithelium was as a rule preserved. Not infrequently small necrosis imbibed with bile.

Comments: The distal portion of the common bile-duct remaining in the form of a canal was but 0.6 cm in length and yet ramified into two ducts immediately before it combined with the abnormal pancreatic duct. Such a case, with the ramified distal portion, is described, although very seldom, in the literature on this subject (*Yasui*'s case). The distal portion in Case 3 was severely narrowed and barely let in a thin bougie. Since the two openings of the distal portion at the inside of the abnormal pancreatic duct were no larger than half a millet-seed, we can easily conclude that the stenosis of the distal portion had not been secondarily due to inflammation, etc., but that the duct must have been congenitally formed narrowly. Therefore two congenital malformations, namely congenital dilatation of the proximal portion of the common bile-duct and congenital stenosis of the distal, as I have pointed out, were actually in existence in this case.

The hole, which was larger than a pigeon egg and was situated at the left lower end of the cyst, and from whose bottom the distal portion of the common bile-duct arose, seems to me to be the formerly narrowed distal portion which had been dilated secondarily after the cyst had been moderately enlarged, because a marked margin suggesting a former valvular infolding could be seen at the entrance of the hole, and because the inside of the latter showed several indistinct circular folds arranged in tiers. This assumption moreover can be maintained by the fact that the cyst wall was especially thinned at the right half of the bottom of the hole.

Quite similar abnormalities in the course of the pancreatic ducts as in Case 2 were confirmed also in this case. Rejoicing to see that my propositions in Clause 14 in "Conclusions" have been actually verified in this case, I will emphasize once more what has been related in that clause.

In Case 3, the right hepatic duct was dilated globularly to the size of

an apple, and such a condition is rarely recorded in the literature on this subject. A single-layered columnar epithelium was found at the inside of the cyst wall, and this also seldom occurs in cases of idiopathic cystic dilata ion of the common bile-duct. In cases of that disease, the contents of the cyst are ordinarily infected secondarily, causing ulceration of the inside of the cyst wall, but they must have been non-infected or but very m ldly infected in this case.

As another complicating congenital malformation, an accessory pancreas of the size of a walnut existed in the subserous tissue of the small intestine about 11 cm distant from *Vater*'s papilla. Such a large accessory pancreas is not commonly found in the autopsy.

Extensive haemorrhage had occurred recently in the right cerebellular hemisphere. In case of idiopathic cystic dilatation of the common bile-duct, the haemorrhagic diathesis is ordinarily raised, as is known to all, according to chronic jaundice or cholaemia, and therefore the operative treatment of that disease is always attended with the danger of operative or post-operative haemorrhage. But such a immense spontaneous haemorrhage in the central nervous system has never been observed in any case of that disease.

Bibliography

1) *Adam, L.*, Idiopathische Choledochuszyste. Ztbl. f. Chir., Bd. 50, Tl. 1, 1923, S. 997. 2) *Akamine, K.*, A case of congenital dilatation of the common bile-duct. Nippon-Gekagakkai-Zassi, Vol. 33, 1932-33, P. 598. 3) *Akiya, Y.*, Choledochus cyst. Ibid., Vol. 27, 1926-27, P. 1848. 4) *Arnolds*, Mannskopfgrosse Retentionszyste des Choledochus. Dtsch. med. Wschr., Bd. 32, Tl. 2, 1906, S. 1804. 5) *Backer-Grøndahl, N.*, Über idiopathische Choledochuszysten. Med. Rev., Bd. 50, 1933, S. 337 (abstr. in Ztorg. f. d. ges. Chir. u. ihre Grenzgeb., Bd. 64, 1933, S. 800). 6) *Bakeš*, Vortrag an der k. k. Gesellschaft der Ärzte in Wien, Sitzung von 1. März 1907. Wien. klin. Wschr., Bd. 20, 1907, S. 298. 7) *Benčević, J.*, Ein Fall sogenannter idiopathischer Choledochuszyste. Liječn. Vjesn., 1928, Nr. 6 (abstr. in Ztbl. f. Chir., Bd. 56, 1929, S. 1661). 8) *Beneke, R.*, Die Entstehung der kongenitalen Atresie der grossen Gallengänge; nebst Bemerkungen über den Begriff der Abschnürung. Universitätsprogramm, Marburg, 1907 (cited from *Böhm, Buzik* and *Giezendanner*). 9) *Böhm, F.*, Ein Fall von kongenitaler Gallengangsatresie mit Gallengangszyste. Ztschr. f. angew. Anat. u. Konstitutionslehr., Bd. 1, 1914, S. 105. 10) *Bohmansson, G.*, A case of cyst of the common bile-duct. Acta chir. scandinav., Bd. 56, H. 5, 1924, S. 440 (abstr. in Ztbl. f. Chir., Bd. 51, 1924, S. 1985). 11) *Bolle, H.*, Ein Fall von idiopathischer Choledochuszyste. Dtsch. med. Wschr., Bd. 48, Tl. 2, 1922, S. 1381. 12) *Bolling, R. W.*, Congenital cyst of the common bile-duct. Ann. of Surg., Vol. 79, 1924, P. 147. 13) *Broca*, Dilatation énorme du canal cholédoque. Bull. et mém. de la Soc. de Chir. de Paris, Tom. 23, 1897, P. 209 (abstr. in Ztbl. f. Chir., Bd. 25, 1898, S. 799). 14) *Budde, M.*, Über die Pathogenese und das Krankheitsbild der zystischen Gallengangserweiterung (sogenannte idiopathische Choledochuszyste). Dtsch. Ztschr. f. Chir., Bd. 157, 1920, S. 364. 15) *Budde, M.*, Über idiopathische Gallengangserweiterungen. Ibid., Bd. 185, 1924,

S. 339. 16) *Budde, M.*, Ein Choledochusdivertikel und seine Deutung. *Virchows* Arch., Bd. 252, 1924, S. 442. 17) *Butters*, Choledochus-Zysten. Dtsch. med. Wschr., Bd. 36, Tl. 2, 1910, S. 1351. 18) *Buzik, J.*, Zur Lehre des angeborenen Verschlusses der grossen Gallengänge. Arch. f. Verdauungskrkh., Bd. 22, 1916, S. 370. 19) *Clairmont*, Diskussion zu *Exner*. Wien. klin. Wschr., Bd. 24, 1911, S. 1616. 20) *Clark, J. H.*, So-called idiopathic choledochus cyst, its pathogenesis and pathology. Report of a case with review of the literature. Internat. Clin., Vol. 1, Ser. 42, 1932, P. 78 (abstr. in Ztorg. f. d. ges. Chir. u. ihre Grenzgeb., Bd. 58, 1932, S. 573). 21) *Djörup, F.*, Über idiopathische Choledochusdilatation. Ztbl. f. Chir., Bd. 61, 1934, S. 428. 22) *Dreesmann*, Beitrag zur Kenntnis der kongenitalen Anomalien der Gallenwege. 1. Hochgradige Erweiterung des Choledochus. Dtsch. Ztschr. f. Chir., Bd. 92, 1908, S. 401. 23) *Ebner, A.*, Idiopathische Choledochuszyste und Purpura haemorrhagica fulminans. Beitr. z. klin. Chir., Bd. 64, 1909, S. 472. 24) *Edgeworth, F. H.*, Case of dilatation of the common bile-duct simulating distension of the gall-bladder. The Lanc., Vol. 1 for 1895, P. 1180. 25) *Eljasberg, M.*, Über eine selbständige Zyste des gemeinsamen Gallenganges, gleichzeitig Beitrag zur sog. weissen Galle. Polska gazeta lekarska, Jg. 3, Nr. 42 u. 43, 1924, S. 617 (abstr. in Ztbl. f. Chir., Bd. 53, 1926, S. 1035). 26) *Elperin, S.*, Ein Fall von angeborenem Defekt des Ductus choledochus aus mechanischer Ursache. Frankf. Ztschr. f. Pathol., Bd. 12, 1913, S. 25. 27) *Erdély, J.*, Die chirurgische Bedeutung der Gallengangszysten. Dtsch. Ztschr. f. Chir., Bd. 209, 1928, S. 65. 28) *Eve, F.*, Large cyst of the common bile-duct. The Brit. Med. Jl., Vol. 1 for 1906, P. 802. 29) *Exner, A.*, Vortrag an der k. k. Gesellschaft der Ärzte in Wien, Sitzung von 10. November 1911. Wien. klin. Wschr., Bd. 24, 1911, S. 1615. 30) *Feyrter, F.*, Über Fehlbildungen der extrahepatalen Gallenwege mit Störung der normalen Hohlraumbildung (Verödung, Enge und zystische Erweiterung) und des normalen Gangverlaufes. *Virchows* Arch., Bd. 271, 1929, S. 20. 31) *Fischel, A.*, Lehrbuch der Entwicklung des Menschen, Julius Springer, Wien und Berlin, 1929. 32) *Flechtenmacher, C.*, Operativ entfernte Choledochuszyste im Ligamentum hepatoduodenale. Wien. klin. Wschr., Bd. 32, 1919, S. 365. 33) *Fowler, R. S.*, Choledochus cyst. Ann. of Surg., Vol. 64, 1916, P. 546. 34) *Frizelle, E. R.*, Idiopathic congenital dilatation of the common bile-duct. The Brit. Med. Jl., Vol. 1 for 1932, P. 610. 35) *Fukamati, R.*, A case of choledochus cyst. Tokyo-Idi-Sinsi, Vol. 1 for 1925, No. 2406, P. 335. 36) *Fukuda, T.*, Zwei Sektionsfälle von Zyste des Ductus choledochus. Nippon-Syokakibyogakkai-Zassi, Vol. 21, 1922, P. 9. 37) *Ghon, A.*, Leber, Gallenblase und Gallenwege, Pankreas. Pathol. Anat. v. *Aschoff*, Bd. 2, 7. Aufl., 1928, S. 857. 38) *Giezendanner, E.*, Beitrag zum Studium der kongenitalen Choledochuszysten. Frankf. Ztschr. f. Pathol., Bd. 38, 1929, S. 150. 39) *Goldammer*, Beiträge zur Chirurgie der Gallenwege. Beitr. z. klin. Chir., Bd. 55, 1907, S. 41. 40) *Hanser, R.*, Gallenblase und Gallenwege. Handb. d. speziell. pathol. Anat. u. Histol. v *Henke* u. *Lubarsch*, Bd. 5, Tl. 2, 1929, S. 748. 41) *Hanser, R.*, Missbildungen der Leber. Ibid., Bd. 5, Tl. 1, 1930, S. 1. 42) *Hayasi, T.*, An interesting case of choledochus cyst. Tyugai-Idi-Simpo, No. 969, 1920, P. 934. 43) *Heidecker*, Idiopathische Gallengangserweiterung. Ztbl. f. Chir., Bd. 55, 1928, S. 610. 44) *Heiliger, J.*, Über die kongenitale zystenartige Erweiterung des Ductus choledochus. Med. Diss. Giessen, 1910 (cited from *Kremer*). 45) *Hertwig, O.*, Die Elemente der Entwicklungslehre des Menschen und der Wirbeltiere, Gustav Fischer, Jena, 6. Aufl., 1920. 46) *Hildebrand*, Geheilte Choledochuszyste. Dtsch. med. Wschr., Bd. 39, Tl. 2, 1913, S. 2224. 47) *Hill, N. H.* & *Ramsay, R. A.*, Cystic dilatation of the common bile-duct. The Brit. Med. Jl., Vol. 2 for 1925, P. 991. 48) *Huber, P.* u. *Lutterotti, O.*, Zur Kenntnis der mechanischen Gallengangserweiterungen. *Virchows* Arch., Bd. 270, 1928, S. 243. 49) *Imai, T.*, Idiopathic dilatation of the common bile-duct. Tohoku-Igaku-Zassi, Vol. 17, 1934, P. 99. 50) *Isawa, T.*, A cured case of idiopathic choledochus cyst. Nippon-Gekagakkai-Zassi, Vol. 30,

1929–30, P. 434. 51) *Iselin, H.*, Gemeinsame Zyste der Gallen- und Pankreaswege. Arch. f. klin. Chir., Bd. 145, 1927, S. 304. 52) *Isii, K.*, A case of cystic dilatation of the common bile-duct. Nippon-Gekagakkai-Zassi, Vol. 22, 1921–22, P. 494. 53) *Isimaru, S.*, On three cases of idiopathic dilatation of the common bile-duct. Ibid., Vol. 31, 1930–31, P. 617. 54) *Isoda, S. & Kameda, U.*, A dissected case of choledochus cyst. Nika-Zassi, No. 390, 1932, P. 2189. 55) *Ito, H.*, On a case of idiopathic dilatation of the common bile-duct. Rinsyo-Igaku, Vol. 8, No. 2, 1920, P. 149. 56) *Idumi, G.*, A case of choledochus cyst. Dikken-Iho, Vol. 9, No. 103, 1923, P. 725. 57) *Janik, A.*, Angeborene zystische Erweiterung des Choledochus. Chir. Klin., Bd. 2, 1929, S. 104 (abstr. in Ztorg. f. d. ges. Chir. u. ihre Grenzgeb., Bd. 53, 1931, S. 460). 58) *Jauregui, P.*, Über idiopathische Choledochuszysten. Rev. Cir., Bd. 7, 1928, S. 536 (abstr. in Ztorg. f. d. ges. Chir. u. ihre Grenzgeb., Bd. 46, 1929, S. 527). 59) *Judd, E. S. & Greene, E. I.*, Choledochus cyst. Surg., Gynecol. & Obstetr., Vol. 46, 1928, P. 317. 60) *Kaira, K.*, On cyst formation of the common bile-duct. Kyoto-Idi-Eisei-Si, No. 164, 1907, P. 4. 61) *Kadikawa, T.*, A cured case of dilatation of the common bile-duct. Idi-Simbun, No. 1263, 1930, P. 1034. 62) *Kambe, N.*, Über idiopathische Choledochuszyste. Arch. f. japan. Chir., Bd. 7, Beih., 1930, S. 74. 63) *Kamiya, M.*, A case of idiopathic dilatation of the common bile-duct. Nippon-Gekagakkai-Zassi, Vol. 32, 1931–32, P. 1494. 64) *Karell, U.*, Über die angeborene zystische Erweiterung des gemeinsamen Gallenganges. Eesti Arst, Bd. 10, 1931, S. 353 (abstr. in Ztorg. f. d. ges. Chir. u. ihre Grenzgeb., Bd. 55, 1931, S. 701). 65) *Kasiwazaki, A.*, A case of biliary cirrhosis of the liver due to stenosis and cyst formation of the bile-duct. Rinsyo-Syonika-Zassi, Vol. 1, No. 3, 1927, P. 45. 66) *Kato, K.*, Cystic dilatation of the bile-duct. Rinsyo-Igaku-Syasin-Dufu, Vol. 8, 1928–30. 67) *Kato, R.*, A cured case of idiopathic choledochus cyst. Therapie, Vol. 5, 1928, P. 632. 68) *Kato, R. & Igarasi, S.*, A cured case of idiopathic choledochus cyst. Arch. f. japan. Chir., Vol. 5, 1928, P. 187. 69) *Kawaisi, K.*, Dilatation of the bile-duct. Nippon-Gekagakkai-Zassi, Vol. 23, 1922–23, P. 1171. 70) *Kawaisi, K.*, A case of cyst of the bile-duct. Aiti-Igakkai-Zassi, Vol. 32, 1925, P. 455. 71) *Kawaisi, K.*, Discussion to *Matida*. Nippon-Gekagakkai-Zassi, Vol. 27, 1926–27, P. 1622. 72) *Kiselev, N.*, Über die idiopathische Erweiterung des Ductus choledochus. Vestn. Chir., Bd. 78–79, 1932, S. 182 (abstr. in Ztorg. f. d. ges. Chir. u. ihre Grenzgeb., Bd. 64, 1933, S. 380). 73) *Kodumi, K. & Kodama, T.*, A case of cystic dilatation of the bile-duct and its pathogeny. Tokyo-Igakkai-Zassi, Vol. 30, 1916, P. 1413. 74) *Krabbel, M.*, Zur operativen Heilung der idiopathischen Choledochuszyste. Beitr. z. klin. Chir., Bd. 130, 1924, S. 159. 75) *Kremer, J.*, Ein Fall einer durch Choledocho-duodenostomie dauernd geheilten echten Choledochuszyste. Arch. f. klin. Chir., Bd. 113, 1920, S. 99. 76) *Kulakoff, A. N.*, Ein Fall von idiopathischer Zyste des Ductus choledochus. Sammlung chirurgischer Vorträge. Festschrift für *P. A. Herzen*. Chirurgitscheskij Sbornik Moskau, 1924, S. 265 (abstr. in Ztorg. f. d. ges. Chir. u. ihre Grenzgeb., Bd. 30, 1925, S. 188). 77) *Kuriyama, S.*, On abnormalities of the bile-duct in children. Nika-Zassi, No. 304, 1925, P. 1519. 78) *Kuriyama, S.*, Demonstration of patients and specimens. Ibid., No. 376, 1931, P. 1334. 79) *Kuriyama, S.*, Demonstration of patients and specimens. Ibid., No. 402, 1833, P. 2063. 80) *Kuriyama, S.*, Demonstration of specimens. Ibid., No. 404, 1934, P. 101. 81) *Kuru. S.*, Über die zystische Erweiterung des Ductus choledochus. Rinsyo-Igaku, Vol. 1, 1913, P. 342. 82) *Lange, K.*, Beitrag zur „idiopathischen Choledochuszyste". Ztbl. f. Chir., Bd. 54, 1927, S. 2287. 83) *Lavenson, R. S.*, Cyst of the common bile-duct. The Amer. Jl. of the Med. Scienc., Vol. 137, 1909, P. 563. 84) *Legg, J. W.*, Note on the cause of the cirrhosis which follows obstruction of the bile-ducts. The Lanc., Vol. 1 for 1877, P. 190. 85) *Matida, T.*, On a case of choledochus cyst. Nippon-Gekagakkai-Zassi, Vol. 27, 1926–27, P. 1622. 86) *Masson, J. C. & Rieniets, J. H.*, Adenocarcinoma and squamous-cell carcinoma in a cyst of the mesosigmoid; choledochus cyst. The Surg. Clin. of North Amer.,

Vol. 11, 1931, P. 743. 87) *Mayesima, J.*, A case of the common bile-duct which is dilated cystically. Nippon-Gekagakkai-Zassi, Vol. 12, 1911–12, P. 109. 88) *Mayesima, J.*, Zur Kasuistik der primären zystischen Erweiterung des Ductus choledochus. Dtsch. Ztschr. f. Chir., Bd. 119, 1912, S. 338. 89) *McConnel, A. A.*, Cyst of the common bile-duct. The Brit. Jl. of Surg., Vol. 7, 1919–20, P. 520. 90) *McWhorter, G. L.*, Congenital cystic dilatation of the common bile-duct. Arch. of Surg., Vol. 8, 1924, P. 604. 91) *Melichow, P. G.*, Zur Frage der idiopathischen Gallengangserweiterung. Russkaja klinika, Bd. 3, H. 9, 1925, S. 74 (abstr. in Ztbl. f. Chir., Bd. 52, 1925, S. 2046). 92) *Mintz, W.*, Über Choledochuszysten. Ztbl. f. Chir., Bd. 40, 1913, S. 1263. 93) *Morley, J.*, Congenital cyst of the common bile-duct: with report of two cases. The Brit. Jl. of Surg., Vol. 10, 1922–23, P. 413. 94) *Nagayo, M.*, Über die Histogenese und Bedeutung der *Langerhans*schen Inseln des Pankreas, und ihre Beziehung mit dem Pankreasdiabetes. Tokyo-Igakkai-Zassi, Vol. 20, 1906, P. 669. 95) *Nakamura, M., Igarasi, H. & Fukusima, S.*, On idiopathic choledochus cyst. The Jl. of Gastroenterol., Vol. 10, 1935, P. 670. 96) *Narabayasi, T.*, Ein Fall einer durch Choledochoduodenostomie dauernd geheilten idiopathischen Choledochuszyste, und ein Beitrag zur Ätiologie. The Jl. of Orient. Med., Vol. 1, 1923, P. 122 & 316. 97) *di Natale, S.*, Contributo allo studio dell cisti del coledoco. Arch. ital. Chirurg., Bd. 23, Nr. 5, 1929 (abstr. in Ztbl. f. Chir., Bd. 57, 1930, S. 674). 98) *Neugebauer, F.*, Zur Kenntnis der idiopathischen Choledochuszyste. Beitr. z. klin. Chir., Bd. 131, 1924, S. 448. 99) *Nisizawa, T.*, A case of dilatation and retention cyst of the common bile-duct due to obliteration of the duodenal papilla. Nika-Zassi, No. 78, 1906, P. 759. 100) *Ogata, T.*, Beiträge zur experimentell erzeugten Leberzirrhose und zur Pathogenese des Ikterus mit spezieller Berücksichtigung der Gallenkapillaren bei der Unterbindung des Ductus choledochus und der Ikterogenvergiftung. Beitr. z. pathol. Anat. u. z. allg. Pathol., Bd. 55, 1913, S. 236. 101) *Ogawa, S.*, A dissected case of choledochus cyst. Nika-Zassi, No. 372, 1931, P. 715. 102) *Oglobin, A. A.*, Die idiopathischen Zysten des Choledochus. Chir.-Propäd. Klinik der Univers. Smolensk., Bd. 9, H. 26 u. 27, S. 177 (abstr. in Ztbl. f. Chir., Bd. 55, 1928, S. 33). 103) *O'Gorman, F. M., Chely, L. & Heyden, C. F.*, Idiopathic choledochus cyst: Report of a case. N. Y. State Jl. Med., Vol. 31, 1931, P. 1196 (abstr. in Ztorg. f. d. ges. Chir. u. ihre Grenzgeb., Bd. 56, 1932, S. 512). 104) *Okuya, H.*, Two cases of dilatation of the common bile-duct. Grenzgebiet, Vol. 2, 1928, P. 813. 105) *Olivecrona, H.*, Un cas de kyste infecté du cholédoque. Acta chirurg. scandinav., Bd. 62, 1927, S. 347 (abstr. in Ztbl. f. Chir., Bd. 55, 1928, S. 1897). 106) *Oxyley, M. G. B.*, Congenital atresia of the duodenal opening of the common bile-duct in an infant, producing a large abdominal tumour. The Lanc., Vol. 2 for 1883, P. 988. 107) *Pamperl, R.*, Zur Behandlung der idiopathischen Choledochuszyste. Med. Klin., Bd. 21, Tl. 2, 1925, S. 1608. 108) *Parker, G.*, Congenital hepatic cirrhosis with obliteration of the bile-ducts. The Lanc., Vol. 2 for 1901, P. 520. 109) *Pfuhl, W.*, Die Leber. Handb. d. mikroskop. Anat. d. Mensch. v. *Möllendorff*, Bd. 5, Tl. 2, 1932, S. 235. 110) *Pfuhl, W.*, Die Gallenblase und die extrahepatischen Gallengänge. Ibid., Bd. 5, Tl. 2, 1932, S. 426. 111) *Popović, B.*, Zystisch-idiopathische Erweiterung des Choledochus. Med. Pregl., Bd. 4, 1929, S. 194 (abstr. in Ztorg. f. d. ges. Chir. u. ihre Grenzgeb., Bd. 47, 1929, S. 838). 112) *Reel, P. J. & Burrell, N. E.*, Cystic dilatation of the common bile-duct. Ann. of Surg., Vol. 75, 1922, P. 191. 113) *Rietz, J.*, Über die normale und abnormale Entwicklung der extrahepatischen Gallenwege. Nord. med. Ark., Bd. 50, H. 1, Nr. 20, 1917 (abstr. in *Schmidts* Jahrb. d. in- u. ausländ. ges. Med., Bd. 328, 1918, S. 19). 114) *Rostowzew, M. J.*, Ein Fall von hochgradiger zystischer Erweiterung des Ductus choledochus. Dtsch. med. Wschr., Bd. 28, 1902, S. 739 u. 758. 115) *Russell, H.*, Case of cystic dilatation of the common bile-duct in a child. Ann. of Surg., Vol. 26, 1897, P. 692. 116) *Saint, J. H.*, Cystic dilatation of the common bile-duct. The Brit. Med. Jl., Vol. 1 for 1932, P. 230.

117) *Sakuma, S.*, On retention cyst of the bile-duct. Okayama-Igakkai-Zassi, No. 181, 1905, P. 49. 118) *Šantručeк, K.*, Sogenannte idiopathische Choledochuszyste. Čas. lék. česk., 1932, S. 1185 (abstr. in Ztorg. f. d. ges. Chir. u. ihre Grenzgeb., Bd. 60, 1933, S. 840). 119) *Sato, M.*, Über die sog. idiopathische Choledochuszyste. Okayama-Igakkai-Zassi, Nr. 443, 1926, S. 1332 u. 1348. 120) *Sato, T.*, A case of cystic dilatation of the bile-duct. Nippon-Gekagakkai-Zassi, Vol. 21, 1920–21, P. 1. 121) *Schloessmann*, Beitrag zur Kenntnis der Choledochuszysten. Dtsch. Ztschr. f. Chir., Bd. 109, 1911, S. 160. 122) *Schürholz*, Ein Fall von sog. idiopathischer Choledochuszyste. Arch. f. klin. Chir., Bd. 118, 1921, S. 91. 123) *Schwalbe, E.*, Die Morphologie der Missbildungen des Menschen und der Tiere, Tl. 1, allgemeine Missbildungslehre, Gustav Fischer, Jena, 1906. 124) *Sebeka*, Ätiologie, Pathologie und Symptomatologie der idiopathischen Choledochuszyste. Casopis lékaruv ceskych, 1927, Nr. 17–20 (abstr. in. Ztbl. f. Chir., Bd. 54, 1927, S. 878). 125) *Seéliger, S.*, Beitrag zur Kenntnis der echten Choledochuszysten. Beitr. z. klin. Chir., Bd. 99, 1916, S. 158. 126) *Sekiguti, S.*, On cyst formation of the common bile-duct. Nippon-Gekagakkai-Zassi, Vol. 13, 1912–13, P. 117. 127) *Sénèque, J.* et *Tailhefer, A.*, Les dilatations congénitales du cholédoque (anciens "kystes idiopathiques du cholédoque"). Jl. de chir., Tom. 33, No. 2, 1929, P. 154. 128) *Sioda, H.*, Discussion to *Sekiguti*. Nippon-Gekagakkai-Zassi, Vol. 13, 1912–13, P. 117. 129) *Simmonds*, Über kongenitale Atresie der grossen Gallenwege. Münch. med. Wschr., Bd. 55, 1908, S. 2565. 130) *Skormin, B.*, Über die verschiedenen Formen des Ikterus im Säuglingsalter. Jahrb. f. Kinderheilk., Bd. 56, 1902, S. 176. 131) *Sternberg, C.*, Diskussion zu *Exner*. Wien. klin. Wschr., Bd. 23, 1911, S. 1616. 132) *Sugaya, T.*, A case of cystic dilatation of the bile-duct. Seikai-Geppo, No. 434, 1918, P. 168. 133) *Swain, W. P.*, A case of cholecystoenterostomy with the use of *Murphy*'s button. The Lanc., Vol. 1 for 1895, P. 743. 134) *Tailhefer, A.*, Dilatation congénitale du canal cholédoque. Bull. et mém. de la Soc. Nat. de Chir., Tom. 60, No. 1, 1934, P. 8. 135) *Takaisi, D.*, Two cases of choledochus cyst. Osaka-Igakkai-Zassi, Vol. 13, 1914, P. 935. 136) *Tanaka, K.*, A case of idiopathic choledochus cyst. Rinsyo-Igaku, Vol. 12, 1924, P. 940. 137) *Tawara, M.*, Two cases of choledochus cyst. Nika-Zassi, No. 370, 1931, P. 480. 138) *Taylor, J.*, Cystic dilatation of the common bile-duct: record of an example. The Brit. Jl. of Surg., Vol. 16, 1928–29, P. 327. 139) *Terada, H.* & *Yagi, Y.*, A case of idiopathic choledochus cyst. Nika-Zassi, No. 367, 1930, P. 2078. 140) *Tudimura, H.*, Über einen operativ geheilten Fall von idiopathischer Choledochuserweiterung. Arch. f. japan. Chir., Bd. 4, 1927, S. 700. 141) *Utido, T.*, A rare case of dilatation of the common bile-duct. Tokyo-Idi-Sinsi, Vol. 55, No. 2751, 1931, P. 2550. 142) *Ugelli, L.*, Sulle dilatazioni congenite del coledoco. Policlinico Sez. chir., Bd. 40, 1933, S. 343 (abstr. in Ztorg. f. d. ges. Chir. u. ihre Grenzgeb., Bd. 63, 1933, S. 651). 143) *Wagner, A.*, Beitrag zur Chirurgie der Gallenwege. Dtsch. Ztschr. f. Chir., Bd. 145, 1918, S. 15. 144) *Waller, E.*, Idiopathic choledochus cyst. Ann. of Surg., Vol. 66, 1917, P. 446. 145) *Walzel, P.* u. *Weltmann, O.*, Studien zur Gallensekretion bei einer Leber-Gallenfistel nach vorausgegangener Totalexstirpation einer sog. idiopathischen Choledochuszyste (Zugleich ein Beitrag zur Choledochusplastik und Cholangiostomie.) Mitteil. a. d. Grenzgeb. d. Med. u. Chir., Bd. 37, 1924, S. 437. 146) *Watanabe, H.*, A case of idiopathic dilatation of the common bile-duct. Nippon-Gekagakkai-Zassi, Vol. 29, 1928–29, P. 416. 147) *Weiss, S.*, Ein seltener Fall von zystischer Erweiterung des Ductus choledochus. Berl. klin. Wschr., Bd. 46, 1909, S. 1843. 148) *von der Weth, G.*, Über kongenitalen Verschluss der Gallenausführungsgänge. Jahrb. f. Kinderheilk., Bd. 97, 1922, S. 259. 149) *Willis, B. C.*, Congenital cystic dilatation of the common bile-duct. Ann. of Surg., Vol. 87, 1928, P. 48. 150) *van P. Wilson, H.*, Choledochus cyst. The Jl. of the Amer. Med. Assoc., Vol. 95, Part 2, 1930, P. 399. 151) *Winterstein, O.*, Zur Diagnostik der Choledochuszyste. Wien. med. Wschr., Bd. 82, 1932, S. 638. 152) *Witzel, O.*, Hemicephalus mit grossen Leberzys-

ten, Zystennieren und einer Reihe anderer Missbildungen. Ztbl. f. Gynäkol., Bd. 4, 1880, S. 561. 153) *Wright, H. W. S.*, Congenital diverticulum of the common bile-duct. Surg., Gynecol. & Obstetr., Vol. 39, 1924, P. 156. 154) *Wyllie, W. G.*, Congenital cyst of the common bile-duct. The Lanc., Vol. 1 for 1925, P. 1342. 155) *Yagi, Y.*, A dissected case of idiopathic choledochus cyst. Nika-Zassi, No. 340, 1928, P. 1635. 156) *Yamanouti, T.*, On cystic dilatation of the common bile-duct. Nippon-Gekagakkai-Zassi, Vol. 22, 1921–22, P. 373. 157) *Yasui, K.*, On idiopathic choledochus cyst. Nika-Zassi, No. 247, 1920, P. 1057. 158) *Ylppö, A.*, Zwei Fälle von kongenitalem Gallengangsverschluss. Fett- und Bilirubin-Stoffwechselversuche bei einem derselben. Ztschr. f. Kinderheilk., Bd. 9, 1913, S. 319. 159) *Young, R. F.*, Diverticulum of the common bile-duct. The Glasgow Med. Jl., Vol. 108, 1927, P. 346. 160) *Zaczek, J. K.*, Eine angeborene Choledochuszyste. Polski Przegl. chir., 6, 1927, S. 639 (abstr. in Ztbl. f. Chir., Bd. 56, 1929, S. 242). 161) *Zimmer, H.*, Idiopathische Choledochuszyste. Ztbl. f. Chir., Bd. 51, 1924, S. 424. 162) *Zinninger, M. M. & Cash, J. R.*, Congenital cystic dilatation of the common bile-duct. Arch. of Surg., Vol. 24, 1932, P. 77. 163) *Zipf, K.*, Über idiopathische Choledochuszysten. Arch. f. klin. Chir., Bd. 122, 1923, S. 615.

Description of Plates

Figs. 1 to **3** are given in the text.

Fig. 4. Case 1. C: cyst. G: gall-bladder. P: pylorus. T: transverse colon.

Fig. 5. Case 1. A thin probe (Pr) is inserted in *Vater*'s papilla. D: duodenum. Pa: pancreas. Otherwise as in Fig. 4.

Fig. 6. Showing the inside of the cyst of Case 2. O: a bougie introduced in the orifice of the distal portion of the common bile-duct. C: a glass tube introduced in the cystic duct. Ch: a glass tube introduced in the opening made at operation (choledochoduodenostomy).

Fig. 7. Case 3. The white arrow demonstrates where the cyst communicates with the duodenum. A: accessory pancreas. Otherwise as in Fig. 4.

抄　錄

特發性總輸膽管嚢腫の病因竝びに成因論知見補遺及び該疾患の3例　元始總輸膽管の生理的上皮性閉塞の時期に於ける上皮細胞增殖の不平等の想定に基く新成因論

(圖版 XXVIII—XXIX)

四ツ柳正造

東北帝國大學醫學部病理學教室(指導　木村教授)

(昭和11年8月7日受付)

余は特發性總輸膽管嚢腫樣擴張症の3檢索例の病理解剖學的所見竝びに文籍的研究に基き，本症の病因に關し，以下の如き結論に到達せり．

1．本疾患の成因に就き，夥多の成因論が提唱せられたりしも，其の大多數は理論

Fig. 4

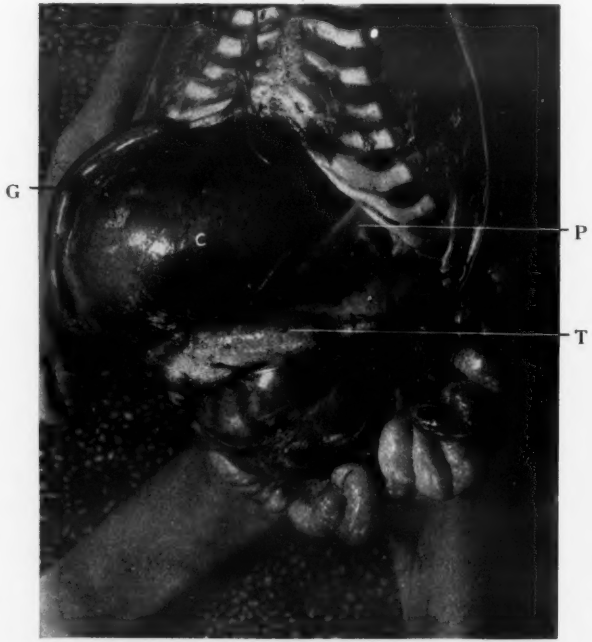
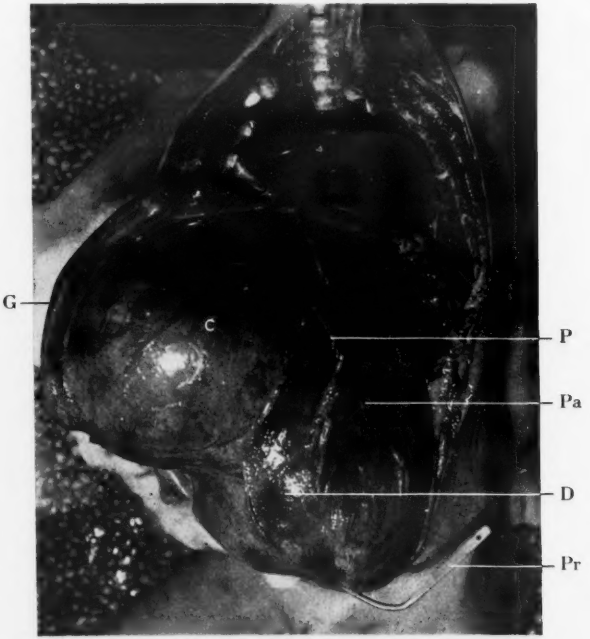


Fig. 5



Syozo Yotuyanagi: Contributions to the Aetiology and Pathogeny of Idiopathic Cystic Dilatation of the Common Bile-duct etc.

Fig. 6

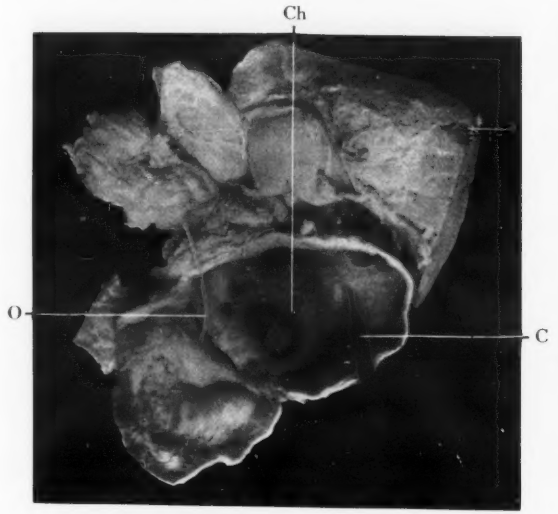
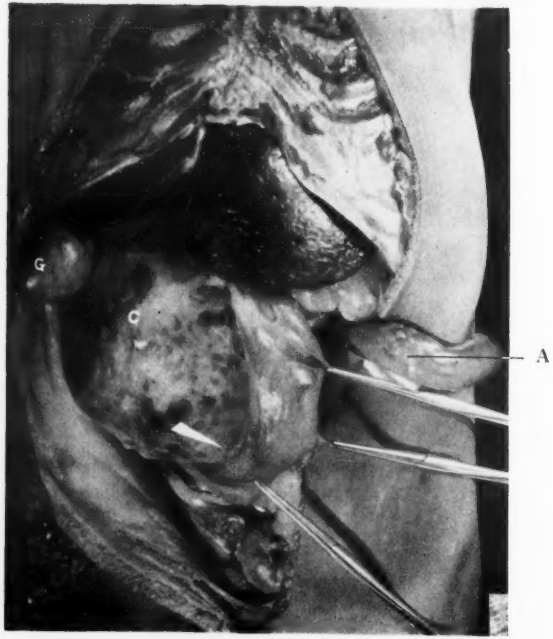


Fig. 7



Syozo Yotuyanagi: Contributions to the Aetiology and Pathogeny of Idiopathic Cystic Dilatation of the Common Bile-duct etc.

的に拒否せらる可く，少數の成立し得る成因論ミ雖も，本疾患例に發見せらるゝ，總べての病理解剖學的所見を解說するに不充分なり．

2．本疾患の症例は一定の共通特徵を示す故，本疾患の成因は多種の原因に因るに非ず，單一の原因に歸せらる可きなり．

3．本疾患は何等かの先天的畸形に因り惹起せらる．

4．本疾患の成立に2個の條件が要求せらる．第1の條件は總輸膽管の限局せられし一部の囊腫樣擴張を可能ならしむる因子にして，此の條件を滿足せしむるは，理論上且つ又事實上，總輸膽管上部の先天的擴張なり．第2の條件は此の先天的擴張を驅つて，一定の症候を發現し，1個の疾患たらしむる因子にして，本條件を滿足せしむるは，總輸膽管下部の先天的狹窄なり．本疾患例にて下部の狹窄は多數の學者に依り等閑視せられたりしも，余が精細なる剖檢記事を記載せる報告例に就き，統計的觀察を試みたるに，實に其の97％にて下部の狹窄乃至閉塞を伴へるを識れり．更に死者の幼若なる程，狹窄が著明に高度なるに留意せり．卽ち下部の狹窄は先天性にして，且つ疾病の成立に重大なる關係あるは自明なり．

5．總輸膽管囊腫樣擴張症の病因は以下の如く解說せらる可し．上述の2種の先天的畸形を有する總輸膽管に於て，下部の先天的狹窄(時には他の偶發的原因)に基き，膽汁が鬱滯し，上部の先天的擴張は增大し，遂に一定の臨牀症狀を發するに到るなり．

6．單に總輸膽管囊腫樣擴張症の際，總輸膽管下部の先天的狹窄乃至閉塞が殆んど恒常證明せらるゝのみならず，吾人は本疾患ミ先天的膽道閉塞症ミの間に多數の移行形の存するを識る．故に兩者は本質的に同種にして，病理解剖學的見地より同一範疇に隸屬せしめらる可き疾患なり．

7．上述より，總輸膽管囊腫樣擴張症の正當なる成因論は，前記の2畸形の成立を同時に說明し得るのみならず，先天的膽道閉塞症の成因を解說し得るものたるを要す．

8．總輸膽管の發生に際し，多數の學者の說ける如く，上皮性閉塞が一時的に發來すミ推測せらる．

9．余は此の上皮性閉塞の時期に於ける上皮細胞增殖の不平等が，本疾患の成立の根本條件たる2畸形を招來すミ思考す．卽ち元始總輸膽管の上部にて增殖の高揚，下部にて低下を推定す．元始總輸膽管の形成に際し，下部の生理的增殖能低下は多數の學者に依り承認せらる，故に余の想定は必ずしも荒唐無稽に非ず．

10．上述の如き上皮細胞增殖の不平等を來せる元始總輸膽管は恰も瓶を倒立せる

が如き外見を呈す．後に上皮性閉塞が解消せば，總輸膽管上部の擴張と下部の狹窄とを來す可し．

11．余の成因論に從へば，特發性總輸膽管嚢腫樣擴張症の全症例の成因を容易に理解し得可く，又先天的膽道閉塞症の成因を說明し得可し．卽ち後者は元始總輸膽管の全長に亙りて增殖能の低下を來せる結果，遂に事實上開孔を得ざるに到りしものなり．

12．余は全實驗例にて膵管の走行異常を證明せり．是は決して，單に個體に種々の畸形が合併して發現すとの意味に解す可きに非ず，元始總輸膽管の畸形，特に下部の異常なる增殖能の低下と因果關係を有するものなり．　(自抄)

原發性肝臟癌に就て

(圖版 XXX—XXXI)

藤 卷 茂 夫

新潟醫科大學病理學教室(主任 川村教授)

(昭和11年8月14日受付)

目 次

緒 言

三浦守治氏は1888年我が邦に於て初めて原發性膽管上皮細胞癌を報告し，次で「ヘパトーム」に關する精細なる記載は山極，貴家兩氏(1911)に依りてなされたり．蓋し「ヘパトーム」は肉眼的竝顯微鏡的所見に於て特異なる位置に在り，且其發生原因に關しては幾多の興味ある點を有するが故に諸外國は勿論本邦に於ても其研究報告は相次でなされ，文獻は甚しく夥しき數にのぼれり．

然るに又佐々木，吉田氏等(1933)はある化學藥品 O-amidoazotoluol に依り實驗的に「ヘパトーム」を發生せしむる事に成功せり．是實に實驗腫瘍學上最近の光輝ある業績にして「ヘパトーム」の本態闡明に對し寄與する處尠からず．されど「ヘパトーム」の發生原因，これと正常肝組織との關係，腫瘍細胞の組織的竝機能的性狀に就ては尙研究の餘地多し．而して本病を地理的分布に基き各地に就て研究するは斯の如き興味ある問題に就て必要なる事項なり．

當病理學教室に於て既に松井氏(1913)は肝癌の1例に於ける轉移竈の稀有なる所見に就て，高泉氏(1922)は小兒に見たる「ヘパトーム」に就き，田中氏(1925)は2例の肝

	番號	解剖番號	住所	年齢性	重量（g）	大さ（cm）	腫瘍部	肝組織
ヘパトーム	I	1985	新潟縣北蒲原	10ヶ月♂	2100	23×19.5×11.8	右葉下面に多數の鷲卵大に至る結節塊磊狀に隆起せり周圍と銳利に界す，灰白黃色乃至暗赤色を呈し稍〻硬く癌腫を見す，壞死軟化竈出血著し	大部分腫瘍組織に占められ極く僅かに存在するのみ，小葉像明かにして帶綠色を呈す，門脈，肝靜脈內には腫瘍栓塞を見る
	II	589	福島縣耶麻	9歲♂	1975	27×22×10	右葉は殆んど一大腫瘍物質より成る其の他多數の結節あり，帶黃灰白色帶赤灰白色，斑狀出血竈あり，軟かし	小葉像不明，門脈，下空竝肝靜脈內には軟かい帶赤灰白色の腫瘍栓塞あり
	III	363	新潟市	39♂	2010	31×13×15	右葉に小兒頭大の腫瘍結節あり⅔を占む，柔軟脆弱，中央部は壞死に陷る，色澤は灰黃色不透明，周邊部は暗綠色なり	右葉は一般に硬變性，硬き暗綠色微細顆粒狀を呈す，實質は結締織によりて多數の分野に區分せられ鬱血，脂肪變性あり門脈下空竝肝靜脈內には軟かき腫瘍栓塞あり
	IV	2000	新潟縣北魚沼	40♂	3030	31×23.9×11.5	麻實大より鷄卵大乃至鷲卵大に及ぶ腫瘍結節多數存在す右葉のものは大なり，帶黃灰白色時に帶綠色，柔軟にして癌腫なし，結締織膜を以て周りと銳利に界す	表面顆粒狀にして帶褐赤色を呈す，小葉像を認む，門脈內に腫瘍栓塞を見る
	V	1149	新潟市	42♂	3600	36×20×12.5	帶黃灰白色の蠶豆大に至る多數の結節あり，左葉臍窪面に鳩卵乃至鷄卵大の結節磊塊狀に相集合	粗大微細顆粒狀を呈す，灰白色小豆大の結節の集合よりなる，小葉像不明，膽管は肥厚し葱形肝蛭を證明す
	VI	772	新潟縣南蒲原	45♀	1440	24×14×8.5	無數の拇指頭大より小豆大の膨隆せる結節簇生し凹凸不平，結節は帶黃灰白色，小葉像僅かに認め得るも二三のものに於て髓樣を呈す	被膜は灰白腱樣に肥厚し纖維性絮片にて蔽はる，尾狀葉は肥大す，點狀出血を見る，下空靜脈の前右壁に三葉の橫位N字形の瓣膜形成あり
	VII	2218	新潟縣東蒲原	47♀	3080	28.5×24×11	右葉臍窪面に拇指頭大より鷲卵大に至る結節あり，大なるは球狀，柄を有し突起す，一部は橫隔膜と癒著す左葉に小鷄卵大のものあり灰白色，暗赤色乃至帶綠色脆弱	表面は平滑なり，割面に肉荳蔻肝を見，黃褐色を呈す，下空靜脈，門脈には綠色脆弱なる腫瘍塊あり
	VIII	433	新潟縣佐渡	51♀	3520	33×21×14	多數の腫瘍結節あり，右葉のものは手拳大に及べり，柔軟にして帶黃灰白乃至暗赤色，中には腫瘍組織の脫落し海綿樣造構あり	表面に纖維性絮片あり，肝組織は暗赤色，下空靜脈竝門脈には腫瘍物質にて栓塞せられたり

表

轉移形成	脾重量(g)	其他の所見	組織的所見	肝組織的所見
腎，膵，副腎，肝門部，胃周圍，後腹膜，氣管側淋巴腺	腫大せず	脾臟內格子狀纖維は輕度に不規則に增殖す	腫瘍胞巢は實質性時に出血壞死の中に胞巢を見る，壞死は輕度，腫瘍細胞は小形，境は明か，核大さ肝細胞に等大，核小體不明．核質多し，組織內に赤血球毋細胞，小淋巴球多し	肝組織內には肝細胞間に美麗なる絲色膽汁圓壔を證明す，肝細胞は萎縮性脂肪肝を呈す
肺，肝門部，氣管側，後腹膜淋巴腺	200	浮腫，尿に蛋白を證明す，「グリコゲーン」顆粒を腫瘍細胞竝其の核內に見る	毛細血管網內の腫瘍胞巢は全く實質性，中央壞死に陷れるものあり，腫瘍細胞は肝細胞と等大，核は 2—3 倍，原形質は明性鹽基性，境界不明，核小體不明，核質に富み，核空胞變あり	グ氏鞘は輕度に肥厚す，こゝに圓形細胞の浸潤あり，肝細胞は多數の脂肪滴を有す
肺	400	黃疸，腹水，浮腫，尿蛋白を證明す		
肝門部淋巴腺	225	腹水を見る，脾臟格子狀纖維は平等に輕度に增殖す，「グリコゲーン」顆粒を腫瘍細胞內に證明す	圓形，多角形の實質性胞巢竝索條形成するものあり，胞巢の周圍は毛細血管に直接す，胞巢の中心壞死に陷れるものあり，腫瘍細胞は肝細胞と等大，鹽基性に染まる，空胞變性著し	增殖せる間質結締織は中心靜脈周圍に證明す，グ氏鞘には圓形細胞の浸潤あり，不規則なる小葉像を認む，肝細胞肥大明かならず
肝門部淋巴腺	220	黃疸腹水，ワ氏反應陽性	多角形の腫瘍胞巢よりなり胞巢相互間を限界するものは毛細血管なり．管腔の形成竝斑狀壞死を證明す	肝組織は萎縮性，硬變性を呈す，膽汁圓壔を見る
〃	450	黃疸，腹水，浮腫，尿蛋白を認む，脾臟格子狀纖維は强く增殖す	肥大せる肝細胞索は漸次其正常索條より胞巢狀に變化す，細胞は鹽基性に染色せられ核も肥大し核質に富み核小體も著明に肥大し核分劃像も見らる．花環狀像あり，星芒，腫瘍細胞內に膽汁あり	間質結締織の增殖甚だしく特に中心靜脈周圍に著し，肝細胞の增生肥大あり所により萎縮性なり．膽汁圓壔を見る
肺	60	出血性腹水，浮腫，腫瘍細胞竝核內に「グリコゲーン」，脾臟格子狀纖維は增稍；强く網狀に增殖す，肺臟轉移結節內には「ヘパトーム」內と同樣，星芒，腫瘍細胞內に膽汁	腫瘍胞巢は圓形乃至長圓柱狀なり或は索條を形成す，間質は毛細管なり時に毛細管は甚だしく擴張す，核分劃多竝單核巨態細胞多し，原形質は紫赤色染，核は大明形核質に富み，核小體不明	小葉內には高度の鬱血を見る間質の增殖なし，肝細胞の肥大なし
肺，大網	120	出血性腹水，尿蛋白を證明す	多角形を呈する腫瘍胞巢の周圍には毛細血管を證明す腫瘍細胞は數倍大のもの等大のものあり，原形質は鹽基性染，核小體は 1—3 個肥大を見る，グ氏星芒細胞，腫瘍細胞內に膽汁色素を認む，核分劃多，單巨態細胞	間質の增加は中心靜脈附近にしてこゝには同時に鬱血を見る，肝細胞の肥大を證明す

	IX	2145	新潟市	52 ♂	3100	28×22.5×13	右葉には無數の結節あり，鶏卵大のものあり，半球狀に隆起す，帶黄灰白色乃至暗赤色，柔軟，壞死軟化竈著明	被膜に結締織絮片あり，微細顆粒狀にして褐赤乃至黄褐色，門脈内に脆弱なる腫瘍塊癒著せり，膽囊は160 cc膽汁容れ，蛭形肝蛭あり
	X	478	新潟市	55 ♂	2800	23×18×16	右葉穹窿面に小兒頭大の腫瘍結節ありて半球狀に膨隆せり，肝組織とは厚い結締織膜によりて境す，灰白黄色乃至暗赤色脆弱壞死軟化竈あり	周圍と纖維性に癒著し，肝組織は赤褐色小葉像僅かに見る表面顆粒狀を呈せり硬し
	XI	207	新潟市	56 ♂	1670	24×15×10	左葉に於て後方に突隆せる手拳大の腫瘍結節を見る，依結節の周圍は結締織膜に依りて肝組織と區別せらる，柔軟，帶黄灰色を呈す	表面凹凸不平粗大顆粒狀を呈す，褐赤色を呈して小葉像不明なり，膽管竝膽囊内には蛭形肝蛭の寄生を見る下空靜脈門脈内に栓塞
	XII	951	新潟縣中蒲原	59 ♂	880	21×12×7	右葉下端に胡桃大の腫瘍結節1個あり，混濁帶黄灰白色，脆弱物質よりなる，所々暗褐赤色を呈す	褐青色を呈し小豆大乃至蚕豆大の結節で凹凸不平，肝實質は小豆大の分野に區劃す，小葉像は不明
	XIII	2210	新潟縣佐渡	64 ♂	2850	29×20×12	右葉は比較的平滑，最高部に鶏卵大柔軟なる結節あり，右葉下面には小兒頭大に至る多數の腫瘍結節あり，暗赤色乃至黄綠色，髄樣脆弱	左葉表面は粗大顆粒狀を呈し硬し，横隔膜と癒著せり，門脈に被膜に襲はれた灰白暗赤色軟かき腫瘍塊附著せり
膽管上皮	XIV	2219	新潟市	30 ♂	1070	24.4×15.5×6.6	右葉の前緣下方に小手拳大灰白色硬靭なる腫瘍結節を認む，割面には灰白黄色を呈せり	部分的に纖維性絮片あり，褐色を呈し小葉像著明
	XV	1307	新潟市	40 ♂	?	?	右葉の右大部分は灰白色塊狀の初生兒頭大の腫瘍にて占有せらる灰白黄色を呈し硬し，中央部に軟化竈あり	表面には纖維性絮片あり，暗，褐色を呈し硬し，膽管は擴張しその中に多數の豌豆大の膽石あり，膽囊は擴張(200 cc)輸膽管は通過障碍
	XVI	116	新潟縣北蒲原	45 ♂	1780	26×14×8.5	右葉の右端に硬き灰白色鶏卵大瘤狀を呈する腫瘍あり，該部は表面より癩痕性に陥凹し，被膜は灰白色なり	被膜は灰白色に肥厚す表面には黄灰白色隆起せる多數の結節附著す，この中に肝は黄色粘稠液竝に蛭形肝蛭を容る，灰白褐を呈し小葉像著明

	13)	黄疸，腹水，ワ氏反應陽性，尿蛋白，脾臟格子狀纖維は不規則に稍；増殖せり	腫瘍胞巣の周圍は毛細血管の龜甲形の細胞も胞巣は時に索條を形成せるもの不同，核小體は1個，原形質に赤染せるもの並鹽基性に染れるものとあり，多核巨態細胞，壞死を見る	グ氏鞘は輪狀に増殖し，圓形細胞の浸潤あり，粗大膽管の増殖，腔内に乳嘴狀に肥厚せるあり，肝細胞の増生肥大毛細膽管内膽汁色素の證明あり
肺，大網	275	黄疸，腹水，浮腫あり，ワ氏反應陽性	廣範なる壞死竈の中に尚毛細血管を圍みて健存せる腫瘍細胞群は島嶼狀に存せり，腫瘍細胞は肝細胞大紫赤色に染まる多核，單核巨態細胞核分剤を證明す	肝實質は輪狀に肥厚せるグ氏鞘に依りて島嶼狀を呈す，小葉の全部或は一部に於て肥大肝細胞あり，圓形細胞浸潤せる間質は再び小葉内に入る
肝門部，後腹膜淋巴腺	70	腹水，浮腫を證明す		
	340	腹水，尿蛋白あり	毛細血管網により小なる腫瘍細胞に分たる索條なるも，中に管腔を有するものと同時に異型的に増殖せる龜甲狀實質性のものとあり單核巨態細胞あり，腫瘍細胞は赤色を調ぶ，壞死竈を見る	グ氏鞘は増殖し，肝實質を輪狀に圍む，間質には圓形細胞の浸潤あり，小葉内には肥大肝細胞は斑狀不規則に見らる
肝門部淋巴腺	50	出血性腹水浮腫あり，ワ氏反應陽性，脾臟格子狀纖維は強く不規則に増殖細纖維が大部分なり	腫瘍細胞は數列に索條を形成して並ぶ，これらは毛細管にて圍まる，腫瘍細胞は大小不整，原形質は肝細胞に比して稍；鹽基性，核小體1—2個にして肥大す，多核巨態細胞，斑狀壞死あり，「グリコゲーン」證明	肥厚せるグ氏鞘は小葉を輪狀に圍繞せり，肝細胞の肥大は見られず
肝門部淋巴腺	140	腹水，浮腫	間質の少量なる腺癌にして時に腔なく實質性のものあり，盃狀細胞，「クティクラ」を證明す，腫瘍細胞は大形にして原形質は淡赤染，廣範なる壞死竈あり	グ氏鞘は増殖し肝小葉を不規則ながら島嶼狀に圍繞す，肝細胞は萎縮性，小葉内粟粒結核結節を見る
腹膜，肋膜，皮膚，頭蓋骨，副腎	125	黄　疸	腺癌の像を呈し，間質に富むこと甚だし，又實質性となるものあり，腔の大なるものには乳嘴狀増殖あり，腫瘍細胞には骰子形のもの多し，核は大形，核質に乏しく核小體不明，間質に出血あり	鬱血著明にしてグ氏鞘の輕度の肥厚あり
肋膜，肝門部，後腹膜，氣管，縱隔實，鎖骨上窩淋巴腺	300	腹　水	胞巣は管腔を形成す，時に實質性のものあり，腫瘍細胞は圓柱狀，圓形，楕圓形色々あり，「クティクラ」を證明す核分剤像あり，乳嘴狀増殖著明，壞死を見る	グ氏鞘の肥厚著明にして殊に粗大膽管周圍に明かなり膽管自己の増殖甚だしく腺腫樣像を呈せり，肥大肝細胞もあり

性癌	XVII	889	新潟市	55 ♂	?	?	右葉の中央部に約鶏卵大硬固，灰白色の腫瘍結節あり，肝組織と明かに界ぜられ胞巣状造構あり	横隔膜と纖維性に癒著す，表面凹凸不平，割面は暗赤色，血量に富む，膽嚢は擴張し250cc膽汁あり膽管，膽嚢内に瓦形肝蛭を證明す
	XVIII	12	新潟市	60 ♀	900	20×13×6.5	右葉の右下部に於て周圍に浸潤性に發育せる鶏卵大の1個の腫瘍塊あり，灰白色を呈し中心に空洞形成あり中に蠶豆大の暗赤褐色の膽石を容れたり	表面には纖維性索片附著す赤褐色を呈し硬し，粗大膽管は肥厚しあるものは胡桃大に肥厚す，總輸膽管は强度に擴張せり

臟「ヂストマ」症に合併せる膽管上皮性癌に就き，塚本氏(1927)は下空靜脈狹窄に因り發生せる「ヘパトーム」を報告せり．而して余は當教室に於て以上5例の外更らに13例の原發性肝癌を得たるを以て既報の5例を合せ18例とし，總括して觀察を試みたり．今玆に其の結果に就て述べんとす．

第一章　實驗例

組織的檢索には Formalin 乃至 *Carnoy* 氏固定を行ひたる標本を Paraffin 乃至 Gelatin 包埋法に依り5乃至10μの切片となし，これに HX-E., Elastica-*van Gieson Bielschowsky* 氏法鍍銀法による格子狀纖維染色，*Best* 氏 Glykogen 染色竝 Azan，染色等を施せり．脂肪を檢するに當りては Formalin 竝 *Ciaccio* 氏固定を行ひたるものに，Sudan III の從來の方法の外に川村，矢崎氏新法を併用し，尙 Nilblausulfat 染色を用ひて脂肪の重屈性を檢索せり．今余の所見全例を表示すれば以下の如し．(第1表)

第二章　統計的事項

I　剖檢總屍數に對する頻度

當病理學教室に於ける總屍數2165體に對して原發性肝癌は18例卽0.83％なり．本邦に於ける原發性肝癌に關する統計的觀察をなしたる諸氏の研究に依れば岡田氏(金大1927)は0.69％(10/1440)，宝氏(朝鮮1932)は0.82％(6/733)，新島氏(京大1925)は0.84％(34/4027)，貴家氏(東大1929)は0.957％(110/11494)，岡崎氏(慈大1915)は1.66％(12/721)にして，山根氏(九大1919)は2.28％(57/2503)を擧げたり．卽吾が新潟地方に於ける頻度は以上の統計中比較的小なる方に屬し，殊に金澤或は朝鮮に於けるものと相似たるを知る．

腹膜竝肋膜播種結成，肝門部，腸間膜，縱隔竇，氣管側淋巴腺	?	腹水を認む	長圓柱狀腫瘍細胞は腔を圍み，これに「クティクラ」緣を證明す，原形質は盃狀細胞の如く透明なり，圓形，骰子形の腫瘍細胞もあり，腔は概して大形壞死を見る	ゲ氏繖肥厚せる中に篦形肝蛭橫斷せられ膽管內に認む，膽管周圍の葡萄狀粘液腺の增殖あり，一般肝硬變を呈するに至らず，膽汁色素あり
肝門部，淋巴腺，後腹膜，副腎	?	黃疸，腹水，浮腫あり	腺癌にして腔を圍む長圓柱細胞は 1 列乃至 2，3 列に竝ぶ，腔は囊狀に擴張し腫瘍細胞は乳嘴性に增殖す遊離緣に「クティクラ」緣を見る，原形質は赤紫色顆粒に乏しく核に空胞變性を見る，間質性出血	靜血竝肝細胞の萎縮あり，ゲ氏繖は輕度に肥厚し，膽管周圍に多數の分葉核白血球圓形細胞の浸潤あり

又獨逸癌研究委員會に於て *Lubarsch* 氏の蒐集したる 97,819 體の解屍中原發性肝癌は 117 體にして 0.12 %に當り，而して米國 *Mayo* clinic に於ける *Counceller* u. *McIndoe* 氏 (1926) の研究に依れば 0.14 %(62/42,276) なり．由是觀之吾國に於ける原發肝癌の頻度は歐米に比し約 6 倍に相當せるを知る．

總癌腫に對する肝癌の頻度　惡性腫瘍の統計的研究は近年大いに注目せらるゝに至り長與氏竝田中氏の報告あり．卽全癌腫中最多數を占むるものは胃癌にして 35 4 %乃至 42.7 %の間に在り．原發性肝癌は東京は 7.9 %，福岡は 16.0 %にして第二位なり．當教室田中氏の調査に依れば全癌腫の 6.8 %は原發肝癌にして第三位を占む．京都は第五位にして 5.5 %なり．卽原發性肝癌は第二乃至第三位にして全癌腫の 6—7 %を占むるものなりと言ひつべし．又歐洲に於ては *Lubarsch* 氏は 9,829 例の癌腫を集め，而して 117 例に原發肝癌を證明し，*Herxheimer* 氏は癌 607 例中 6 例卽約 1 %に是を見たり．從て本邦に於ては歐洲に比し，原發性肝臟癌は 6 乃至 7 倍多し．

肝臟附屬器に發生せる癌腫との比較　膽囊癌，總輸膽管癌竝原發肝癌の例數を見るに *Herxheimer* 氏は 53:14:6，*Hansemann* 氏は 25:2:4，*Friedmann* 氏は 22:2:1，*Nobiling* 氏は 9:5:6 なり．當教室の 2165 體の剖檢例中 16:7:18 の割合なり，卽本邦に於ては膽囊癌は原發肝癌と略ゝ同數を示すに反し歐洲に於ては何れも膽囊癌は遙かに多數を占めたり．

原發竝續發生肝癌との比較　歐米に於ける統計を見るに原發肝癌は全肝癌の 1.5—5 %位なり．卽 *Hansemann* 氏は 1.5—2.5 % *Counceller* u. *McIndoe* 氏は 2.3 %，*Herxheimer* 氏は 3 %，*Pleitner* 氏は 5 %を擧げ肝癌の大部分は續發性なるかの觀を呈せり．然れども山根氏は原發肝癌は全肝癌の 38 %に當ると云ふ．余も亦兩癌腫の比較は興味ありと信じ檢索せる處，續發性肝癌は總屍數 2165 體に對し 52 例を得たり．從て原發肝癌は全肝癌に對し 21.21 %なり，該數は外國に於ける者に比し甚しく

相違せる所なるも，益〻原發性肝癌の歐米に比し遙かに多數に出現するてふ事實の證左たるべけん．

Hepatom と膽管上皮性癌との比　原發肝癌に關する各研究者の Hepatom 及膽管上皮性癌の實驗例の數及其比率を表示すれば下の如し．(第2表)

第　2　表

研究者	Hepatom	膽管上皮性癌	膽管上皮性癌と肝癌との比	研究者	Hepatom	膽管上皮性癌	膽管上皮性癌と肝癌との比
			%				%
Egzel 1901	99	17	14.63	貴家 1929	83	27	24.54
岡崎 1915	10	2	16.67	*Herxheimer* 1930	300	95	30.0
新島 1925	19	4	17.39	*Goldzieher* 1911	14	7	33.33
山根 1919	45	12	21.05	藤卷 1935	13	5	27.78
岡田 1927	147	40	21.39				

卽膽管上皮性癌の全肝癌に對する比は 14.6％より 33.3％に當れり．從て肝癌に於ては Hepatom は膽管上皮性癌より其頻度は多く2乃至5倍に達しをれり．

II　年齡竝性別

年齡　余の實驗例中 Hepatom 13例にては，生後より10歲まで2例，11—30歲までの間にはなく，31—40歲まで2例，41—50歲まで3例，51—60歲まで5例，61—70歲まで1例なりき．次に膽管上皮性癌に於ては30歲のもの1例，40—50歲まで2例，51—60歲まで2例なりき．卽兩種癌腫を通じて，年齡的差異中注目すべきは Hepatom に於ては旣に小兒期に出現するものなるに反し，膽管上皮性癌は老年期に至れば次第に高率となること，今之れを文獻に鑑みるに貴家氏(1929)の110例の肝臟癌の統計を見るに Hepatom は1—10歲まで10例，10歲を超ゆれば次第に減少し，次で30歲以後に至れば漸次增加しをれり．*Herxheimer* 氏に依るも10歲までは10％を見るに反し10—20歲間6％，20—30歲間5％と減少するも，30歲以後は漸次增加しをれり．卽余の實驗例も兩氏の成績に略〻一致し，10歲までは高率なるに10—30歲間に於て其の發生は低率を示しをれり．次に貴家氏の膽管上皮性癌に關する統計はその27例中最も多きは50—60歲間にして10例を見たるも，この年齡期の前後には次第に減少しをれり，されど老年期に多きは疑ひなきことにして，又余の結果もこれに一致しをれり．

性別の關係　兩種癌腫に分かちて觀察する時は，Hepatom 13例中男子は10例，76.93％，女子は3例，23.07％，膽管上皮性癌5例中男子は4例，80％，女子は1

例，20％なりき．貴家氏は Hepatom に於ては 78.3％(65/83)は男子にして膽管上皮性癌に於ては男子は 66.6％(18/27)，其の他の統計ミしては Hepatom に於ては男子は夫々 68.4％(*Eggel* 氏)，77％(*Herxheimer* 氏)，膽管上皮性癌に於ては男子は 52.9％(*Eggel* 氏)，55％(山極氏)なり．

以上の諸報告を綜合すれば原發性肝癌も亦他の癌腫に於けるが如く男子に於ては女子に比して遙かに優數を示しをれり．但し玆に興味ある點は 10 歳以下の小兒に於ける Hepatom にして，この關係相異にし或は略ゝ相半するものミするもの(山極，*Castle* 氏等)及び貴下氏の如きは寧ろ女子に於て多數を占め，其の比は 3:1 なりミ．更らに膽管上皮性癌に就ては男子に多きも，Hepatom に比して女子に多數見らるゝは諸家の說一致しをれり．されぞ *Eggel* 氏は略ゝ 1:1 の關係にありミ．

III 黃疸竝腹水

黃疸 Hepatom 13 例中黃疸の證明せられたるもの 5 例(38.46％)，膽管上皮性癌 5 例中 2 例(40％)なりき．卽肝癌總數 18 例中黃疸 7 例，38.88％なり．文獻上には黃疸を有するもの肝癌全體ミして *Herxheimer* 氏は 58％，*Eggel* 氏は 61％，貴家氏は 62％，山根氏は 67％を擧げをれり．

次に黃疸の發生原因に就て余の例にては XV を除ける他の 6 例(III，IV，V，IX，X，XVIII)に於ては孰れも總輸膽管は通過性なりき．從てこの際果して肝臟機能障碍に由れるものなりやは不明なるも，恐らく肝內細小膽管の腫瘍物質により壓迫を蒙れる結果起りたるものなるべし．尙組織的檢査の結果注意すべきは臨牀上黃疸を見ざる I，VI，XVII に於ても肝組織內に膽汁色素を認め，更らに黃疸を有する X，XVIII に該色素を證明せざりしこミなり．

腹水 余の肝癌 18 例中腹水を證明せるもの 15 例．83.33％なりき．內 Hepatom は 84.6％(11/13)にして，膽管上皮性癌は 80％(4/5)なり．文獻によれば *Eggel* 氏は 58.5％，山根氏は 69.6％，*Herxheimer* 氏は 70％を伴へりミ，又岡田氏の本邦に於ける症例を蒐集せる結果は肝癌 185 例中 168 例に腹水を伴ひ，其の內 Hepatom 93％，膽管上皮性癌 82.5％なりミ．而して腹水の原因を尋ぬるに余の例に於ては甚だ屢ゝ肝硬變の合併あり，又門脈枝內には腫瘍栓塞の多きこミより見れば，門脈管流域の狹隘を來たし爲めに腹水を惹起せるものなり．又膽管上皮性癌に於ては其の他所謂癌腫性腹膜炎を有する XV，XVII，XVIII に於ては腹水はこの腹膜の癌性炎症に原因ありミ考ふるを至當ミす．又腹水は時に出血性のこミあり(VII，VIII，XIII)．VII に於ては腫瘍結節は柄を有して腹腔內に突出し，其の一部は被膜を缺き，明かに該部より出血せ

しこさを指摘し得.

次に浮腫を有するものは8例にして Hepatom は7例，膽管上皮性癌は1例なりき．又尿中に蛋白を證明せるものは6例にして，浮腫さ同時に蛋白尿を有するものは Hepatom のみに見られたり．これ恐らくは，肝細胞乃至腫瘍細胞の異常機能及び其の潰滅に由る分解産物が腎臟に作用し，茲に病變を惹起せるものならんか.

IV 轉移形成

Hepatom に於ては一般に肝外轉移は稀なりさせらる，其の理由さして *Mirolubow*, *Saltykow* 氏等は腫瘍細胞は血流に逆行して門脈に達し，之れに由りて中心靜脈は屢〻腫瘍物質により閉塞せらるゝを以て肝内に擴がり得るも肝外に出るこさ困難なるが爲なり．更らに Hepatom に於ては肝内を灌流する血管の配列竝に緩徐なる血流の爲，腫瘍物質が毛細内穿破の容易なるこさも肝内傳播をして益〻好都合ならしむさ述べられり．今 Hepatom に於ける轉移形成を門脈系，肝靜脈系，淋巴系に分かち述べんに

門脈系 腫瘍細胞は好んで門脈内に破入す，而して其の脈管内に於て中心性及び末梢性に増殖し又血行に依り他の部に腫瘍栓塞乃至血塞を形成す，この栓塞乃至血塞は吾人が肉眼的にも屢〻觀察し得るものなり．余は實驗例13例中門脈内に腫瘍栓塞を肉眼的及顯微鏡的に證明せるは VI，XII を除く外11例にして84.6％なりき.

肝靜脈系 次に腫瘍組織は肝靜脈内にも穿破するこさあり，從つて下空靜脈内に腫瘍栓塞を見るこさあり．即余の13例中6例に於ては斯の如き轉移は下空靜脈内栓塞さして認め其の率46.15％なりき．該6例の中 XI を除く他の5例には同時に肺轉移を見居れり．之れ下空靜脈に破入せる腫瘍は早晩心臟を經て肺に到達し，其處に栓塞性轉移を發生するは了解し易き所なり，この際心臟内の轉移形成は *Culpepper & Haam* 氏(1934)は右心耳に之れを見たりさ報告せるも甚だ稀有のものなり．更らに又腫瘍細胞は肺毛細管を通過し大循環系内に送られ諸臟器内に同樣の轉移を來すこさあるは可能にして，余の I に見るが如く，腎，膵，副腎に轉移結節を證明しあるは之れなり.

淋巴系 余の例に於て肝門部淋巴腺に轉移結節を見たるものは6例(I，II，IV，V，XI，XIII)，後腹膜淋巴腺3例，大網2例なりき．尙時には遠隔なる淋巴腺にも轉移の來得るこさは I，II に於ては氣管側淋巴腺に轉移を認めたるにて明かなり．肝門部淋巴腺轉移は又 XIII に於けるが如く組織的檢査の結果腫瘍細胞が血行を介して到達せる像を呈するものあるは注目に價すべし.

之れを要するに余の實驗例を以てすれば Hepatom の肝臟外轉移は今迄人の考へた

るが如き稀有のものに非ざるを示しをれり．但し肝外に於ける轉移は他の內臟の癌腫に比し其の大さ小にして看過せられ易く，組織的に之れを證明し得るものあるの差あるのみ．而して斯の如き現象は既に先人の述べられたるが如き腫瘍組織と門脈及び肝靜脈との關係に重きを置くべきも，これ腫瘍細胞の性狀に基くものにして而も斯の如き肝臟外轉移は早期に起らず寧ろ晚期に於て發生するに基くものならんか．

膽管上皮性癌に於ては全く前者と趣きを異にし，血管系を介して轉移形成を見ること甚だ少なく，主として淋巴系に依るものとせらる．されど姑に興味あるは Hepatom に見ざりし肋膜播種結節を3例(XV, XVI, XVII)に於て(60%)，腹膜播種結節を2例(XV, XVII)に於て(40%)，橫隔膜の癌性肥厚を2例(XVI, XVII)に於て(40%)實驗せしことなり．之れ恐らくは被膜下淋巴毛細管を介しての轉移に依れるものにして，又稀には被膜を穿破し其の表面に出でたる眞の意味に於ける播種も存在するものならん．次に淋巴系を介しての淋巴腺の轉移は部位的淋巴腺に4例(XIV, XVI, XVII, XVIII)，80%を見たり，後腹膜淋巴腺2例(XVI, XVIII)40%，其の他 XVI にては鎖骨上窩，氣管側，縱隔竇淋巴腺への轉移を見，更らに副腎に證明せるもの2例(XV, XVIII)，VXII は肺臟，皮膚，頭蓋骨に轉移を來せり．斯の如く膽管上皮性癌の轉移に於ては Hepatm の其れに比して廣範なる轉移形成を見るは兩者の間の差違の大なるを語るものなり．然れども之れは一般的の事にしての例外は勿論あり，卽 XIV は膽管上皮性癌なりしも二三の肝門部淋巴腺にのみ轉移が見をれり．而して該例は結核屍にして剖檢上副所見として始めて肝癌を發見せしものなり．

本例の轉移形成の僅少なりし理由を考へんに，腫瘍の組織的所見より見れば相當に發育進行しをるものなるも，未だ之れに依る症候を呈するに至らざりしを以て，其の發育は未だ高度に達せざりし爲なること，更らに結核と癌腫の拮抗作用に就て尙議論せらるゝ所なるも，本例に於ては兩者間の拮抗作用の存在も顧慮に入るべきものならんか．

第三章　肉眼的所見總括

I　形態的分類

原發性肝癌は以前結節型竝瀰蔓性型の2型に分類せられ，英國に於ては，これに對し Tubera circumscripta, 竝 Tubera disseminata なる稱呼を附せり．其後 *Hanot et Gilbert* 氏は Cancer nodulaire, Cancer massiv, Cancer avec cirrhose の3型に分類せり．然るに該3型中前2者と雖も肝硬變を伴へる場合は甚だ多數にして Cancer

avec cirrhose なる名稱はやゝもすれば正鵠を缺くの嫌あり．玆に於て *Eggel* 氏(1901)の結節狀，混塊狀竝瀰蔓性の3型は最も適合せる分類法ニ云ふべし．原發性肝癌の多くは結節狀に現はるゝを常ニし，第3の瀰蔓性型は最も少數ニせらる．

余の實驗例中 Hpatom 13例に於て結節狀を呈せるものは9例(I, II, IV, V, VII, VIII, IX, XII, XIII)にして69.23％なり．何れも肝臟の右又は左葉に亙りて多數の結節は密在せるに反し混塊狀を呈せるものは3例(III, X, XI)にして23.07％に當り，右葉に小兒頭大の結節1個ニ其の周圍に小なる僅かの轉移結節を認むるなり．瀰蔓性型に屬する者は1例(VI)のみにして7.69％，肝臟は普通大にして表面著しく粗大乃至微細顆粒狀を呈してをれり，膽管上皮性癌(XIV 乃至 XVIII)の全例ニも腫瘍結節は右葉に1個の結節狀を呈して單發せり．

II 肝臟重量竝周圍との癒著狀態

肝臟は概して其の大さ竝に重量を增加せり．

實驗例中最大重量を示せるはVにして3,600g を算せり，其の甚だしく腫大せる肝臟を報告せるものには貴家氏の 10,000g 竝 *Bruzelius* u. *Schwink* 氏等の 14,000g あり．又余の例に於ては乳兒竝小兒(I, II)に於てすら夫々2,000 及 1,975g にして成人肝臟重量の限度 1,600g (1400±200g) を超えたりき．爾他11例中該限度を超えて增大せるもの9例(III, VI, V, VII, VIII, IX, X, XI, XIII) にして84.6％なり．又13例中15.4％は普通大乃至其以下にしてXIIの如きは880g に縮少せり．斯かる肝臟の縮少は肝硬變ニ密接なる關係を有するなり．肝臟の縮小せる報告例を見るに，貴家氏は 440g *H. Meyer* 氏は肝臟は約1/2に縮小せるもその重量は1,200g なりきニ．

今 Hepatom の重量竝長さ，幅，高さの中何れが最も增大せるやに就き生物測定學的に觀察し以下の如き結果を得たり．(第3表)

第 3 表

Hepatom	M	σ	C
重量 (g)	2532.08±181.08	934.1 ±128.61	36.89±8.13
長さ (cm)	27.91± 0.79	4.08± 0.56	14.62±2.78
幅 (cm)	18.76± 0.85	4.34± 0.60	23.14±4.71
高さ (cm)	11.55± 0.44	0.28± 0.31	19.72±3.83

今正常成人の肝臟平均重量 1268.42±17.37g (楠本氏)竝 Hepatom のMニの差を見るに 1263.66±181.91g を得，同樣にして幅の增加は 3.03±0.87cm，高さのそれは 4.36±0.46cm にして，長さの差は殆ニなかりき．以上のことより最も大ニなるもの

は高さにして，次が重量なり，幅は稍〻増加し，長さは變化なしと言ひ得べし．

次に膽管上皮性癌に於ける肝臟の平均重量は1,250gなりき．

原發性肝癌中横隔膜との癒著を見たるものは18例中10例なり．Hepatom 13例中半數(VI，VII，VIII，IX，X，XIII)は癒著を示しをれど其程度は輕微なるか，部分的のものなりき．反之膽管上皮性癌にては5例中4例(XIV，XV，XVII，XVIII)にこれを見たれど一般にその癒著は高度なりき．卽膽管上皮性癌に於ては轉移狀態より論ずるも悪性にして，周圍を侵襲すること Hepatom より多きは當然なるも又 Hepatom の場合に於ても，病竈は比較的肝内に限局することは云へ，屢〻横隔膜との癒著を見ることと多し．

III 腫瘍結節の狀況

Hepatom の腫瘍結節は概ね圓形を呈し其大さは種々雜多を極む．VIに於ける結節は豌豆大乃至指頭大にして，XIIIは胡桃大なり．然れどもこの2例以外の余の肝癌は孰れも大なる結節を有し，鷄卵大のもの3例(V，XVI，XVII)，鶯卵大のもの7例(1，II，IV，VII，IX，XVII，XVIII)，手拳大のもの3例(VIII，XI，XIV)にして時に小兒頭乃至初生兒頭大に及べり(III，X，XII，XIII)，就中III，X，XIに於ける混塊型に屬するものは甚だ大なり．

腫瘍の占位は大多數のものに於て右葉に在りて，余の18例中主腫瘍の右葉のみに存するものは10例(III，IX，X，XII，XIII，XIV，XV，XVI，XVII，XVIII)にして，左葉にのみあるものは唯XIのみにして，殘りの7例(I，II，IV，V，VI，VII，VIII)は全葉に亙りて存在せり．兩葉に結節を見る場合もVを除く他の6例の如く右葉の腫瘍結節は常に左葉に於けるものより大なりき．更らに結節は肝臟の穹窿面及び下面に同時にあるもの多し．されど又特に下面にのみ結節の著明のものあり(I，XIII)．結節は一般に肝表面より半球狀に窿起し塊磊狀を呈し，或は腫瘍塊は球形に突窿し柄を以て肝臟に附著せるものありき(VII)．

又 Hepatom 13例共に腫瘍結節は特異なる色澤を有し，帶黄灰白色を呈し渾濁せる脆弱物質より成れり．而して13例の Hepatom 中4例(III，IV，V，VI)を除く他のものにては，結節は又同時に暗赤色にして出血性なり．出血竈の特に著明なりしはI，VIII，Xなりき．時に結節は綠色を呈しIII，IV，V，VII，XIIIの如きは然り．就中IV，XIIIは美麗なる明性帶綠色の結節を無數に有せり．

反之膽管上皮性癌にては結節はXVのみは帶黄灰白色にして，これを除き他のものに於ては總て灰白色を呈し而して出血竈は發見せられざりき．

次に腫瘍結節の硬度に就て見るに Hepatom に於けるものは概して脆弱物質より

なり大なる結節を有せるⅢ，Ⅶ，Ⅷ，Ⅸ，Ⅹ，Ⅺは中心壞死に陷りて柔軟なりき．又Hepatom 全例に於て腫瘍結節の表面に於て癌臍の形成を見ざりき．膽管上皮性癌は間質の量大なるため硬度從て大なりき．腫瘍塊の中心壞死を見たるはⅩⅤ，ⅩⅧの2例なりき．

更らに結節の境界に就てはHepatomの全例に於て結節周圍は灰白色不透明なる結締織被膜によりて肝組織と鋭利に界せらる，該結締織膜は通例肝硬變のため增殖せるグ氏鞘と直接關係づけらるゝものなり．されど散在性の小結節は門脈枝を栓塞しそのため周圍と鋭利に區別せらる．其の他Ⅸに於けるが如く被膜は結節の全周を圍繞することなく一部に於てこれを缺如し直接肝組織を壓迫せる像を呈せるものあり．膽管上皮性癌はⅩⅣ，ⅩⅥ，ⅩⅦ，ⅩⅧの如くこれに反し周圍に浸潤性に發育を營めり．

第四章　顯微鏡的所見總括

Ⅰ「ヘパトーム」

Hepatomに於ける腫瘍細胞の大さは多數例に於て肝細胞大を超え，Ⅵ，Ⅶ，Ⅷ，Ⅸ，Ⅻに見るが始く肝細胞の數倍に達するものあり．又Ⅷ，Ⅸ，Ⅹ，Ⅻに於ては一定の大さなく大小不同なりき．肝細胞と略ゝ等大のものも證明せらる(Ⅱ，Ⅳ，Ⅹ，Ⅻ)，2例の小兒例に於ては(Ⅰ，Ⅱ)寧ろ肝細胞より小なりき．

原形質は全例に於て肝細胞に比し明性にして顆粒性に乏しく，原形質の染色態度を見るにHXの色を比較的多くこれる鹽基性に染色せるものはⅡ，Ⅳ，Ⅶ，Ⅷ，Ⅹ，Ⅻにして，赤染(酸性)せるものはⅥ，Ⅻ，同時に兩者を混ぜるものはⅨに於て見るべし．Hepatomの腫瘍細胞が鹽基性色素に親和力を有すと主張する學者は多し，*Winternitz, Goldzieher* u. *v. Bókay, Heukelom van Siegenbeek, Wegelin, Landsteiner* 氏等は然り，*Mirolubow* 氏は又腫瘍細胞は寧ろ好酸性たることを說けり．而して腫瘍細胞の化學的性狀の變化はこれ等細胞の染色上に於ける性狀を種々に變化すべきは當然ならんも，其の本態は不明なり．又Ⅷ，Ⅸ，Ⅹには腫瘍細胞に2種ありて大多數のものに於ては鹽基性に染色すれども他のものに於ては比較的赤色調を帶び明性の度も大なりき．このものに於ては核質は稍ゝ少量なるに拘らず核小體は著しく肥大せり．これ正しく繁殖力旺盛なる幼若細胞にして肥大肝細胞を思はしめ，*Adler* 氏の明性細胞に一致するものなり．其他原形質內にはⅡ，Ⅳ，Ⅶ，Ⅷ，Ⅸ，Ⅹ，Ⅻ，Ⅻに於けるが如く空胞變性を證明せり．

又Hepatomの腫瘍細胞の個々の境界はⅠ，Ⅳ，Ⅸに於ては比較的明かなれども概

して明かならず，VI，VII，VIII，X，XIII に於ては細胞體融合し *Renon, Gérandel* 氏等の見たるが始き細胞融合物を證明せり．

次に核の性狀に就ては常に其の大さを增し VI，VII，IX，XIII の如きは正常肝細胞の4乃至5倍に肥大せり，又 II，IV，VIII，X，XII に於ける核の大さは2乃至3倍，I に於けるものは略〻肝細胞に等大なりき．文獻例に於て核の著しく大ミなれるものあり，*Stromeyer* 氏は肝細胞核の6倍，*Znieniwicz* 氏は8倍大ミなれるものを報告せり．核質の量は Hepatom の總ての例に於て大なりき．このこゝは多數の學者の一致する所なり．

核小體は VI，VIII，IX，X，XIII に於ては1個稀に2個を認めX を除くこれら4例にては孰れも核小體の肥大著明なりき．

核は又多く集合し巨態細胞を形成するものあり，VI，IX に於ては單核巨態細胞を有するも XII，VIII，IX，X，XII，XIII は多核巨態細胞を認めしむ．VII，VIII，X に於ける巨態細胞は一般に腫瘍組織の發育旺盛なる部に見られたり．これ核分裂に際して原形質の分裂作はざりしもの卽發生上進行性のものに屬せしめ得るものにして，かの腫瘍の陳舊性竈內又はこの附近に存在せる一定數の細胞癒合により成れる退行性のもの(IX，XIII)ミ區別せらるゝなり，*Landsteiner* 氏は巨態細胞を多數の肝癌に於ける顯著なる成分の一つに擧げたり，而して多核肝細胞は旣に正常肝組織に於て出現するものにして，且臟器の再生に際しては巨態細胞の形成せらるゝに注目せば，肝癌に巨態細胞を見るは不可思議ミするに足らざるを示唆せり．*Goldzieher* u. *v. Bókay* 氏等は Hepatom 14例中12例に巨態細胞を見たるも7例の膽管上皮性癌に於ては1例も見ざりき．核分裂像は II，IV，VI，VII，VIII に證明するを得たり．

核は又種々なる退行變性たるを示せり，卽核の縮小濃染せるものは I を除く全例に經驗せられ，其の外空胞變性を示せる例も甚だ多し，(I，II，IV，VI，VII，VIII，IX，X，XII，XIII) 又 VIII には著明なる核分解の像を證明し得たり．

II 膽管上皮性癌

膽管上皮性癌に於ては膽管の稍〻粗大なる部より發生せるもの(貴家氏分類甲型)にありても，或は小葉間膽管より發生せるもの(同乙型)に於ても腫瘍胞巢は中に管腔を有せり．

腫瘍細胞の性狀に就いては XIV，XV は多角形乃至橢圓形にして，XVI，XVII，XVIII に於ては腫瘍細胞は圓柱狀乃至長圓柱狀より成り，同時に圓形，多角形細胞を混じ居れり．腫瘍細胞の大さは正常小葉間小膽管上皮細胞を多少超ゆるものより2倍大位に達せり．原形質は明性にして，XV に見るが始き微子形，多角形細胞にありてはその核の

周圍に僅かに認めらるゝも，圓柱狀細胞に在りては核は細胞の基底部に存し，腔に面する側に於てXIV，XVI，XVII，XVIIIに見るが始く Cuticularsaum を證明せり．又XIV，XVI，XVIIに於ては腫瘍細胞內に腸管に見る盃狀細胞の始き觀を呈せるものを混じおれり，これら盃狀細胞は Azan 染色標本に於て稍〻强く青色に著染せるを見たりき．肝癌に於て粘液を生ずる盃狀細胞に似たる癌細胞を有する例は初めて *Bonnet* 氏(1902)に依りて報告せられ，氏はこれを祖先歸へりと見做し，肝細胞が元來腸管葉より分離發生せるものなるを以て，これが胎生狀態に復歸し粘液を生ずるに至りしものならんと說明せり．然れども其の後 *Landsteiner* 氏は膽管上皮細胞竝其附屬腺は生理的狀態に於ても粘液樣物質を生じ得るより，(大膽管には屢〻見出さるゝもの)これは膽管上皮性癌に屬すべきことを證明せり．

核は一般に大形，核質は中等量にして，核構造は明かに認めらるゝも核小體はXIV，XV，XVI，XVIIIの如く不明のもの多く，又XIV，XV，XVIIIに於ては核の空胞變性を示し居れり．其外核の縮小濃染は例外なく見られ，更らに核分裂像の著明なりしはXVIのみにして，巨態細胞は何れの例にも認め得ざりき．

次に膽管上皮性癌の管腔の小形なるものはXIV，XV，XVIにして，殘りの2例(XVII，XVIII)に於ては管腔は比較的大にして囊腫狀に擴張し，中に剝離せる腫瘍細胞竝白血球を混じ居れり．全例に於て腫瘍細胞の腔內に乳嘴性增殖を營めるを見たり，從てXIV，VIII，XV，XVI，に於て見るが如く腫瘍胞巢は時に實質性なりき．

III　壞死竝出血

又腫瘍組織內に壞死を證明せるは Hepatom 所檢10例中VIを除くI，II，IV，VII，VIII，IX，X，XII，XIIIなり，壞死の輕微なりしはI，IV，XIIIにして他の6例は中等度乃至高度の壞死を示せり．特にVIIは間質も同時に壞死に陷れり．組織的には一般に壞死と腫瘍結節の大さとの間には一定せる關係存せず，卽I，IV，XIIIに於ては甚だ大にして且多數に結節を有すれど，僅微の壞死を證明せるのみなりき．

膽管上皮性癌の所檢5例中XIV，XVI，XVIIの3例に於て腫瘍組織の壞死を見たり．XV，XVIIIには間質內に出血を認めたるも壞死は證明せられざりき．

第五章　腫瘍組織の其の他の形態的竝機能的性狀

I　組織學的構造

從來の研究者の組織學的分類を見るに *Kaufmann* 氏は原發性肝癌を三型 Alveolärtypus, Karcinom mit Balken u. Schlauchtypus, Adenocarcinom に分てり，而

して前二者は肝細胞より發生せるものにして第3型は膽管上皮細胞癌ニし，第1型は腫瘍胞巢は間質結締織によりて圍繞せらるゝものを云へり．反之 *Goldzieher* u. *v. Bókay* 氏等(1911)は Hepatom には次の3型ありニ云ふ，Trabekulärer Typus, Medullärer Typus, Alveolärer Typus これなり．前二者に於ける間質は毛細血管にして第1型は腫瘍細胞は索條に配列するもの，第2型は實質性胞巢にして，第3型は間質は結締織より成れるものを云ふ，更らに膽管上皮性癌に對して同氏等は Carcinoma basozellulare, Adenocarcinom, Carcinoma simplex cubozellulare を區別せり．之より曩に *Eggel* 氏(1901)は發生學的竝組織形態學的見地より肝癌を分類して肝細胞より來るもの(1型)，及毛細膽管より生ずるもの(2型)ニなし，而して各型は更らに各々 Carcinoma salidum ニ Carcinoma adenomatosum に區別せらるゝものニせり．

以上述べたるが如く肝臟癌の組織學的構造は種々多樣なりニ雖も，其の間に共通せる性質あり，之れを Hepatom ニ膽管上皮性癌(Cholangiom)ニに大別し得べし．先づ膽管上皮性癌に於ては孰れも腺癌の像を呈し，而もXIV，XVは腺細胞癌にして，XVI，XVII，XVIIIは圓柱細胞性癌に屬せしむるを得．

次に Hepatom に就て述べんに，VI，X，XIIIは一般に生理的肝組織に類似し腫瘍細胞は二三列乃至數列に配列し索條を形成し相互に連絡しをるもの(正型的發育)，次にI，II，V，VIIIに見るが如く腫瘍細胞は實質性に集合して多角形乃至橢圓形の胞巢をなし而して之等胞巢は毛細血管網に由りて夫々區劃せらる(異型的增殖)．或はIV，VII，IX，XIIの如く同時に兩型の發育狀態を示せるものあり．更らに異型的組織像を呈せるものゝ中には腫瘍胞巢の中に於て管腔を形成するものあり．實驗例中これを最も著明に出現せしめたるものはIIなりき，この例にては同一結節中に龜甲形の實質性胞巢竝其の中に管腔を形成せるものニ併存し，該胞巢を形成せる細胞は骰子形にして數層に配列せり，腔は必ずしも胞巢の中心に存せず，又其の大さの甚だ大なるものあり．腔のあるものは淡赤染同質性物質を容れたり．尙VI，VII，IX，XIIに於ても管腔形成を見たるもIIに於けるものニは趣を異にせり．この內IXに於けるものは小なる管腔にして腫瘍細胞の數倍大なるも，VI，VII，XIIの腔は甚だ細小なりき．

以上の管腔形成に就ては山極氏はこれに花環狀像なる名稱を與へたり．*Herxheimer* 氏はこれを以て肝臟の再生現象特に所謂急性黃色萎縮或は肝硬變に際して見らるゝ僞膽管乃至管腔形成に相當するものニなせり．又肝細胞が曾て經過せる低分化の狀態への逆行にして膽管を模倣せりニなすものあり(*Heukelom v. Siegenbeek, Wegelin*)．更らに余のVIIに於けるが如く癌結節中に管腔が稍ゝ擴張し膽汁を以て鬱積するこニ

あり，貴家氏はこれを以て毛細膽管擴張による瀦溜囊胞の一種なりとせり．されど他方に於て Hepatom 內管腔は腫瘍の中心壞死により生ずる軟化囊腫に屬するものなりとなすものあり (*Mirolubow*)．而してかゝるものゝ腔壁は不規則にして腔內に膽汁に非ずして細胞破壞物を容れ居れり，余の實驗例 II，IV の如きこれなり．其の成因に就ては小なる壞死竈が中心に發生することより察すれば，該部は周圍の毛細血管に距り位し從て榮養不良なるに基くものならん．卽 Hepatom 胞巢內に發生する管腔形成は，一は腫瘍細胞間に存在する毛細膽管の出現顯著になりたるものにして，山極氏の花環形成に相當するもの及び他は壞死に依りて生ずる軟化空洞これなり．

肝癌が肝細胞乃至膽管上皮細胞より發生するとすれば，其腫瘍細胞は夫々母細胞が有する形態學的及機能的諸性質を多少に拘らず具有すべきものならんことは腫瘍學上想像し得べき事柄なり，余は次にこの點に就き聊か述ぶる所あらんとす．

II 膽汁分泌

Ribbert, *Mirolubow*, *Saltykow* 氏等は腫瘍細胞內竝腔內に膽汁色素を證明せり．其の他多數の學者に依り肝外轉移竈に於ても該色素は認められたり．而して之れ腫瘍細胞自身に膽汁生產能力の存するを證するものにして，又この事實は Hepatom は肝細胞より發生せるを立證するに足るものなりと述べ居れり．又 Hepatom の轉移竈內膽汁色素形成に就き *Lubarsch* 氏は之れを肯定するに反し，*Aschoff* 氏は轉移竈に於ける腫瘍細胞にして左程變化せざる間は血液內既存の膽汁色素を攝取し得べきは當然なればなりと反駁せり．瀧澤氏 (1934) は Hepatom 例の肝外轉移竈に於ける星芒細胞內に該色素を證明し，之れを以て *Kupffer* 氏細胞よりの生成なりと考へおれり．

余の實驗例を通覽するに，3 例 (VI，VII，VIII) に於て余は腫瘍細胞內に綠黃色大小滴狀の膽汁色素を證明せり．VI にては同時に殘存肝組織內にも (肝細胞，毛細膽管內) 該色素を認めたり，本例には輕度黃疸ありき．VII に於ては微細なる腫瘍胞巢內 Rosetten の腔內にも膽汁圓塊を見，且腫瘍細胞は勿論，*Kupffer* 氏細胞內にも更らに肺臟の轉移竈に於ける腫瘍細胞竝 *Kupffer* 氏細胞內にも膽汁を認めたり．然れども肝組織內にはこれを見ず，臨牀的にも黃疸を認めざりし例なり．VIII は腫瘍細胞，*Kupffer* 氏細胞兩者共滴狀乃至顆粒狀の膽汁を有し居れども黃疸はなかりき．腫瘍細胞內膽汁色素に就てはこれが腫瘍細胞の生產に依れるものなりやに就ては議論の岐るゝ所なり．然るに余の I，V，IX，XVI の 4 例に於ては腫瘍細胞內には膽汁色素は陰性なりしに拘らず，肝組織內にこれを證明せり．卽腫瘍組織內膽汁色素が鬱積性に基くものとすれ

ば，これは黄疸の有無及其の程度に關係せざるべからず．然るに黄疸を有する例に於て腫瘍組織内に全然膽汁色素を證明せず，又反對の例あるを見るに於ては，膽汁色素の有無は腫瘍細胞が健全なる限り自主的にして，自個の機能に關係するものならざるべからず，夫れ故に腫瘍化の程度により，或る例に於ては腫瘍細胞はこの膽汁分泌機能を全然喪ふも，他の場合に於ては尙これを保持するも少しも怪しむに足らざるなり．

次に *Kupffer* 氏星芒細胞内膽汁形成に就て余は VII に於て上述の如くこれを認めたり．この際血液内膽汁量は *Meulengracht* 8 にして生理的限界を超えず，同時に肝組織内には黄疸を何等證明せざりしに拘らず，肝外轉移竈の腫瘍細胞竝 *Kupffer* 氏細胞内には美麗なる綠色乃至黄褐色の膽汁色素を認め得たり．これ網狀織内被細胞は病的の場合に於ても Bilirubin 形成に關與するものを證明するものなり．

III 脂肪竝「グリコゲーン」

原發性肝癌中 Hepatom は其の腫瘍細胞内に，その母細胞に似て，脂肪を含有するは周知のこゝなり．本田氏 (1911) は小兒 Hepatom に就きて脂肪檢索の結果を報告し居れり，之れに依れば，この脂肪の種類は Lipoid にして，この外に中性脂肪は可なり多量に存し．極少量に重屈性脂肪を間質内出血竈に見たりゝ云ふ．Hepatom 腫瘍細胞の脂肪變性の本態に關しては *Prym* 氏 (1912) は之れを脂肪沈著乃至脂肪浸潤ゝ解し居り，且脂肪變性に向ふ道程は，腫瘍細胞は肝細胞ゝ全く軌を等しくするものなりゝ述べ居れり．更らに岡田氏 (1927) は Hepatom 腫瘍細胞内の胞體，核内に空胞ゝして認められしものは Sudan III に黄赤色を呈して著染せるを認め居れり．當病理學教室に於て，高泉氏 (1922) は Cholesterinaemie を有せる小兒の Hepatom (余の II) に於て脂肪を腫瘍細胞原形質の外に核内にも證明せり，又肝組織の *Kupffer* 氏細胞ゝ同時に腫瘍胞巢の毛細管網壁の内被細胞内にも脂肪を見，その性は重屈性の Cholesterinester なりきゝ．其の他 Hepatom 腫瘍細胞の單なる脂肪變性に就き述べし個々の例あるも，これら脂肪に就き總括して論じたる報告に接し得ず，仍て余は實驗例に就て此の點に向ひて檢索せり (第 4 表)．

余の 9 例の **Hepatom に就て見るに**腫瘍細胞は何れも脂肪變性を示し居れるも，其脂肪沈著の程度は種々多樣なり，Sudan III にて VIII の如く瀰蔓性淡黄色に染まれるもの，乃至 I の如く黄赤色微細顆粒狀のものより，大小滴狀を呈して多量に存し，腫瘍細胞の原形質を充塡するに至るものあり (II, IV, VII, IX, X, XIII)．殊に高度に脂肪變性に陷りたるものは II, IV, VII, XIII なりき．又玆に注意すべきは核の脂肪變性にして II, IV, VII, XII に見られ，その甚だしく著明なりしは II, VII (この 2 例は同時に Glykogen

第 4 表　脂肪所見

肝癌	番號	腫瘍部 腫瘍細胞 S_{III}	$S_{新}$	C	$C_{新}$	Nilb.	腫瘍部 壞死竈 S_{III}	$S_{新}$	C	$C_{新}$	Nilb.	腫瘍部 間質 S_{III}	$S_{新}$	C	$C_{新}$	Nilb.	肝組織 肝細胞 S_{III}	$S_{新}$	C	$C_{新}$	Nilb.	肝組織 星芒細胞 S_{III}	$S_{新}$	C	$C_{新}$	Nilb.
「ヘパトーム」	I	±	+	±	+	−						++++	++++	++	++++	±	++++	++++	++	++++	+					
	II	++++ K++	++++ ++++	± +	+ ++	± ±	++++	++++	±	+	+	星芒 ++	++++	±	+	+	++++	++++	+	++	+	++	++++	+	++	+
	IV	++++ K++	++++ ++++	± ±	+ ++	± ±											++	++++	+	++	±					
	VII	++++ K++	++++ ++++	+ +	++++ ++	± −	++++	++++	+	++	±	++	++++	+	++	++++	++++	++++	±	+	±	++	++++	±	+	±
	VIII	±	++	±	+	±	+	++++	+	++	+	++++	++++	+	++++	++++	+	++++	+	++	+					
	IX	++++	++++	++	++++	+	++++	++++	+	++	+						++	++++	±	+	−					
	X	++	++++	+	+	++	++++	++++	+	++	++						±	++	±	+	±	+	++	±	+	−
	XII	++ K+	++++ ++	± ±	+ +	++ ±											++	++++	++	++++	++	++	++++	++	++++	±
	XIII	++++	+++++	+	++++	++						+	++	±	+	−	++	++++	+	++	+					
腺管上皮性癌		K‥‥核					腔内																			
	XIV	±	+	−	±	−	++++	++++	+	++	+	++++	+++++	++	++++	+	++++	++++	+	++	±					
	XVI	±	+	±	+	−	+	++	+	++	+	+	++++	+	++++	±	±	+	−	+	+	++	++++	+	++++	++
	XVII	±	+	±	+	−	++++	++++	+	++	+	++	++++	+	++	−	+	++++	+	++	+					
	XVIII	−	±	−	±	−						±	+	±	+	+	±	+	±	+	±	±	++	±	+	±

も核内に見らる)にして，**濃赤色大小の脂肪滴**は全く核を遮蔽せり．而も興味あるはVIIにして核には甚だ高度の脂肪變性を見たるに拘らず，その原形質は殆んど侵されざるものありき．

間質脂肪は肥厚せる結締織纖維間に遊離性乃至遊走細胞内に濃赤色顆粒乃至滴狀に存在し，これを認めたるは4例(I，VII，VIII，XIII)なりき．次に壞死竈を有する部に於ては腫瘍組織に何れも黄赤色脂肪顆粒を大量に見たり．

Sudan III 新法に於ては脂肪の出現は更らに顯著にして，脂肪變性極弱度なりしVIIIに於ては黄赤色微細顆粒狀に染まれり．その他の例に於ても舊法に比し遙かに大量に脂肪を證明し得たり．

次に *Ciaccio* **氏固定標本**にては，腫瘍細胞はVII，IX，X，XIIIに於ては稍〻著明に黄赤色顆粒狀乃至滴狀に脂肪を證明すれどもI，II，IV，VIII，XIIに於ては極微量に認めたるのみ．*Ciaccio* 氏固定新法に於ては舊法に比し著明に脂肪顆粒乃至脂肪滴を認めたり．尙核脂肪に就ても *Ciaccio* 氏舊法にては僅かに見得たるも新法に由りて稍〻多量に證明するを得たり，間質脂肪は4例共 *Ciaccio* 氏法にて陽性を示せり．壞死竈に於ける脂肪は僅かに認め得たるが(II，VII)新法に於て甚だ著明なりき．

Nilblau 染色標本に於ては腫瘍細胞の脂肪は淡赤色，赤色，紫赤色より暗青色に至る種々著染の顆粒竝塊狀を呈し居れり．重屈性脂肪も所々之れに混じ，就中正十字を呈する Cholesterinester は IX，X，XII，XIIIに認められたりき．核脂肪は青色より淡赤色迄の雜色染滴狀を呈し，中に僅かの重屈性脂肪を見る．間質脂肪には4例中2例に於て甚だ多量に Cholesterinester を證明せり．壞死竈脂肪にはII，VIII，IX，Xはこの中に Cholesterinester を混じおれり．

肝組織を見るに全例共に多少に拘らず脂肪變性を示せり．中心性脂肪變性はII，IV，VIIの3例にして，又II，VII，X，XIIの4例に於ては *Kupffer* 氏細胞に脂肪沈著を證明せり．而して肝細胞竝星芒細胞内脂肪は大體に於て中性脂肪より成りしも尙僅かに Lipoid を混有し，IIの星芒細胞には Cholesterinester を認めたり．

膽管上皮性癌に於ける腫瘍細胞内脂肪は Hepatom に比し遙かに少し，卽XVIIにては極微量か或は殆んど證明せられず，他の3例XIV，XVI，XVIIにては僅かに脂肪顆粒乃至脂肪滴を見たりしのみ．*Ciaccio* 氏固定に依りて檢するに大部分は Lipoid より成れり，但し腫瘍胞巢に於ける腔内には相當量の Cholesterinester を證明せり．膽管上皮性癌に於ける壞死竈にも亦脂肪を證明し得，大部分は Lipoid より成り，Cholesterinester なく又中性脂肪を僅少なりき．間質脂肪も亦 Lipoid を混有すれど

大部分は中性脂肪なり，XVIIIの間質には Cholesterinester を認めたり．

肝組織内には脂肪變性は僅少にして *Ciaccio* 氏固定に於て陽性のもの多かりき．

以上の脂肪所見よりして Hepatom 腫瘍細胞竝肝細胞の脂肪の消長を見るに，腫瘍細胞の脂肪變性少なき VIII，X に於ては肝組織にも亦脂肪は少量なりき．反之腫瘍細胞の高度に脂肪變性を示せる II，IV，VII，XIII に於ては肝細胞にも亦大量の脂肪を證明し得たり，然れども一般に腫瘍組織は肝組織に比して，より高度に脂肪變性に陷り居れり，唯例外をなせるは I なり．玆には脂肪肝を呈すれども腫瘍細胞には極少量の脂肪顆粒を見たるのみなりき．Hepatom 腫瘍細胞內脂肪の生成が外因性或は內因性なりやの解決は困難なるも上述の如く腫瘍細胞竝肝細胞に於ける脂肪の消長は略〻相平行せる事實より鑑れば，余は *Prym* 氏と共に Hepatom 內脂肪は外因的生成に由るものなりと思考せんとす．

次に Hepatom に見らるゝ廣範なる壞死竈は著明に脂肪變性に陷るものなり．これら脂肪中には，Hepatom 腫瘍細胞に比すれば，Cholesterinester の出現遙かに多きを知り得たり．核脂肪に就ては II，IV，XII に於ては核は高度の脂肪變性を示し居りしが，この3例は同時に核の退行變性を伴ひ居りしものなり．されど核に空胞變性を見たる VIII，IX，X，XIII に於ては核の脂肪變性は明かならざりき．

又膽管上皮性癌の脂肪所見よりすれば Hepatom は概して中性脂肪を見るに反し，膽管上皮性癌は稍〻 Lipoid より成る傾向を有するを知れり．更らに間質脂肪の出現は膽管上皮意癌にては Hepatom よりも多く見られたり．

Hepatom 腫瘍細胞內の Glykogen の出現に就ては其の成績は一定ならず．中村氏 (1908) は膽管上皮性癌に於て其の細胞中に Glykogen 顆粒を麗しく染色し得たり．然るに對照材料に於て同要約の下に陽性なりしに拘らず，Hepatom 例に於て陰性なりしことより Glykogen の存在は決して其の腫瘍の原發地を定むるに價値を有せざるものとせり．貴家氏 (1908) も Glykogen の證明は必ずしも Hepatom に特異とするに足らざるを述べ居れり．

余の Hepatom I，II，IV，VII，IX，XIII の6例は剖檢時に於て *Carnoy* 氏固定を使用せる材料に就き *Best* 氏 Karmin 染色法を施せるものにして，他の3例 (VIII，X，VII) 竝膽管上皮性癌の3例は 10% Formalin 固定に就き檢査せり．其の結果は4例 (II，IV，VII，XIII) に於て其の腫瘍細胞內に顆粒性 Glykogen を見たり．II，VII にては脂肪と共に腫瘍細胞の原形質のみならず核內にも之れを證明し得たり．II に於ける Glykogen の出現部は腫瘍胞巢の周邊部卽毛細血管壁にして脂肪の出現部位と一致せり，されど

脂肪は更らに壞死部にも證明したれごも Glykogen はこゝには認め得ざりき．他の2例に於ては脂肪竝 Glykogen の沈著部位に就き一定せる關係なし．膽管上皮性癌に於ては其の腫瘍細胞内には Glykogen の證明を見ざりき．

組織内 Glykogen の證明は死後の時間竝其の檢査方法如何に關係するを以て，其の存否の判斷には大いに注意を要すべし，現今 Glykogen 證明に於て最も適當ご見做され居る *Carnoy* 氏法にては，余は Hepatom 腫瘍細胞内に可なりの程度に於て Glykogen を證明し居れり，この余の成績より見れば，Hepatom の腫瘍細胞内には比較的多く Glykogen を現はすも，膽管上皮性癌の腫瘍細胞内にはこれを證明せざるは，矢張り其の母細胞の性狀に依るものならん．されごこれを逆に應用し之れに依り其の發生母組織を判定するには大なる注意を拂ふべきは勿論なり．

IV 間 質

Hepatom の間質が毛細血管なるこごを重要視したるは *Wegelin*，山極，貴家氏等なり．又毛細血管内被細胞が轉移竈にも亦常に見出さるゝこごに對し *Adelheim* は之れを腫瘍細胞の有する血管形成能力に歸せしめたり．次に腫瘍組織内 *Kupffer* 氏星芒細胞の增殖に就ては唯松井，岡田氏等の報告例あるのみ．松井氏(1921)は Hepatom 組織内に明暗兩腫瘍細胞の存在を認め，暗性細胞を以て肥厚せる星芒細胞なりごせり．岡田氏(1927)は腫瘍胞巢内に核の小にして核質に富み，原形質は蜂窩狀を呈せる多角形の細胞群を認めたるが，該細胞は星芒細胞の增殖を主ごし，これに尙小血管内外被細胞の增殖も關與せるものならんごせり．

Hepatom 内格子狀纖維の發生に就ては，仁藤氏(1910)は該纖維は良く發達し，肝臟に於けるご等しく毛細管内被細胞より發生するも，膽管上皮性癌に於ては格子狀纖維の發生を伴はずご云ひ，*Adelheim* 氏(1913)に依れば，Hepatom に於ける格子狀纖維は毛細血管を纖細網狀に圍繞し，屢〻細胞の間を纏絡し居り，而して該纖維の證明は Hepatom 診斷上重要なりご述べ居れり．

余は Hepatom 9例，膽管上皮性癌3例に *Bielschowsky* 氏鍍銀法を施し該纖維を檢せるに，Hepatom の全例に於て增生せる結締織内の黃褐染し纏絡せる膠基纖維中に，格子狀纖維は暗黑色染し，太き强靭なる纖維ごして，直線狀に走行し居るも，腫瘍胞巢に近くに從ひ其の太さを減少し，纖細なる纖維ごなり居れり．更らに放射狀纖維に比すべきものを胞巢周圍の毛細血管壁に沿ひて認め，尙5例(I，IV，VIII，X，XIII)に於ては格子狀纖維は更らに纏絡纖維ごして胞巢内に侵入し，腫瘍細胞を不完全に圍繞し居れり．されご放射狀纖維竝纏絡纖維共に肝組織の夫れに比すれば，其の發育良

好ならず.

膽管上皮性癌に於ては腫瘍間質内に該纖維は腫瘍胞巢を繞りて甚だ良好なる發育を見たるも腫瘍細胞間には殆んど證明せられざりき. (第5表)

第　5　表

肝癌に於ける格子狀纖維							
		腫瘍部			肝組織		
		肥厚結締織	放射狀纖維	經絡纖維	グ氏鞘	放射狀纖維	經絡纖維
「ヘパトーム」	I	++	++	±	++	+++	++
	II	+++	++	−	++	+++	++
	IV	+	++	+	++	+++	±
	VI				++	++	+
	VII	++	++	−	+++	+++	+++
	VIII	+++	++	+	+	+++	++
	IX	++	+	−	+++	++	+
	X	++	++	+	+	+++	++
	XII	++	+	−	+	+++	+
	XIII	++	+	+	+++	+++	++
膽管上皮性癌	XV	+++		−	+	+++	++
	XVI	+		±	+	+++	++
	XVII	++		±	+	++	+

第六章　肝癌の發生論

肝癌の場合に於ても發生機轉を論ずるは他の腫瘍に於けるが如く困難なることなり, されど實質性肝癌 Hepatom に於ては之れが屢〻肝硬變と合併し居るを以て, この際當然顧慮すべきはこの兩者の發生學的關係なり. この事實を初めて提唱せしは *Rosenblatt* 氏 (1867) なり. 今肝癌が硬變と共存する割合を文獻に徵するに, *Herxheimer* 氏は 90 %, *Eggel* 氏は 86.4 %, *Ewing* 氏は 85 %, 山極氏は 74.75 %なりと云ひ, 何れも肝癌發生が肝硬變と如何に密接なる關係を有するかを指示し居れり. 而して肝癌發生に關し共通せる事項は肝細胞の再生的機能にして, 肝細胞の再生現象に就ては *Kretz* 氏 (1902) 以來肝硬變の一特徵と見做され居れり. 山極氏は Hepatom は常に初めは腺腫として發生し徐々に腺腫性癌に變ずるものとなし, 貴家氏は結節狀增生は殆んど常に肝癌の發生母地なりと謂へり.

余の Hepatom VI, X, XII に於ては臨牀上, 上腹部緊張感竝膨隆, 足背浮腫, 腹水ありて肝硬變として診療せられたるものなりしが, 剖檢の結果肝癌と同時に肝硬變が認められたり. この中 VI に於ける Hepatom は初期のものと認むべきものなりき. 而

してこれら結節中增生せる肝細胞結節にては該細胞が漸次核の大さを增し，核質に富み徐々に癌細胞に移行し居る初期癌結節を現示し居れり，卽本例は肝硬變が先行性病變ニしてあり，之れに肝癌が續發せるものなるこニ疑なし．更らに本例は鬱血性肝硬變にして，增生結節ニ共に多數の腫瘍結節の散在せるものなりき．

移行像の問題は當然肝癌發生の多中心性ニ關聯すべきものなり．山極，長與，貴家，*Landsteiner*, *Adelheim*, *Huguenin*, *Goldzieher* u. *v. Bókay*, *Mirolubow*, *McIndoe u. Counceller* 氏等は何れもこの多中心性發生說に左袒せり，余のVIの肝表面は凹凸不平にして無數の拇指頭大乃至小豆大の膨窿せる結節簇生し，特に主腫瘍ニ認むべき陳舊竈に遭遇し得ざりき．この肉眼的所見竝前記組織的所見より考ふる時は本例の腫瘍結節は同一發育時期にあるものゝ如く，寧ろ多中心性に一時に多數の場所に於て發生したるものニなすを至當なりニ信ず．

然れごもこの說に反對し *Ribbert*, *Wegelin*, *Lissauer* 氏等は肝靜脈內に腫瘍栓塞の見出さるゝ事實よりして，腫瘍物質の血管內穿破に依れるものなりニし，單中心性發生を主張せり．*Herxheimer* 氏も單中心性說を信じ居れり．而して多中心性發生論者の見たるものは多く毛細血管內栓塞性轉移に外ならず，且他の多くの腫瘍結節ニは無關係に局所性に極初期結節を證明し得たりニする人あるも，吾人の知り得る點は肝細胞より腺腫形成に至る直接の變化を見るに過ぎず．又斯かる極初期竈に於て之れの惡性化の確證を得るに困難なりニ述べ居れり．

旣に出來上りたる腫瘍結節を以て其發生狀態を認め得べからざるは明かにして，而して之れらに於ては其の發生の單或は多中心性なりやは勿論論じ難し，然れごも肝硬變に際して，多發性結節狀增生竝腺腫形成等を見るが如き特殊なる條件の存在する場合に於ては，余は前揭VIの如くいかに之れを精査するも轉移ニ見做し難く，其の發生の原發性多中心性を信ぜざるべからざる初期癌の存在するは確實なりニ信ず．

次に肝癌ニ肝硬變ニの合併率に就て檢せるに，余のHepatom 13例中肝硬變の共存せしはI，II，VIIを除く10例にして76.92％に當る．もし10歲以下の小兒例（I，II）を除外せば實に90.9％の頻度を得べし．尙組織的に檢し得ざりしは2例（III，XI）なるも，肝表面には粗大乃至微細顆粒狀凹凸ありて肝硬變性變化を示し居れるは疑なし．又Vは組織的に肝硬變を明かにし得たるも，硬變の種類は不明なりき．硬變を見ざりしVIIは肝小葉に於て急性鬱血像あれごも，グ氏鞘の肥厚を見ず，之れ下空靜脈竝門脈に生じたる腫瘍栓塞に原因せる肝臟に於ける局所性鬱血にして，肝臟の他の部に於ては鬱血は輕度乃至殆んご認められざりき．

今之れを硬變の種類に於て見るに，判明せるもの7例中萎縮性肝硬變3例(X, XII, XIII)，萎縮性竝膽管性肝硬變の結合型ニ見做すべきもの1例(IX)，竝鬱血性肝硬變3例(IV, VI, VIII)なりき．而して余は又諸家の唱ふる前述の癌前驅性病變ニ見做し得べき肝組織の增生を硬變を有する7例中萎縮性肝硬變3例(IX, X, XII)竝鬱血性肝硬變2例(VI, VIII)合計5例に於て證明せり．更らに之れら5例中萎縮性肝硬變例IXに於ては，輪狀を呈する小葉內に肝細胞の腺腫樣像を證明し得たり．夫れ故に組織的に肝細胞の增生乃至肥大を明かに證明せざるは唯2例を數ふるのみ．

又3例の鬱血性硬變中原因の明かなりしはVIのみにして，他の2例は不明なりき．VIは下空靜脈に纖膜の形成を見，惹ては高度の鬱血性硬變を來せるものにして興味あることゝ信ず．

以上の所見より肝癌の發生に關して論ぜんに，先づ *Laennec* 氏萎縮性肝硬變の頻度を觀察すれば，以下の如し．

第6表　諸家の調査による肝硬變の頻度

著者	場所	剖檢例	硬變例	陽性率	著者	場所	剖檢例	硬變例	陽性率
Förster	Berlin	3,200	31	1.0	*Askanazy*	Genf	7,089	284	4.0
Rössle	Jena	1,000	15	1.5	*Ophüls*	California	3,000	166	5.5
Blumenau	Frankfurt	12,761	198	1.6	可知，翠川	本邦各大學	18,813	332	1.77
Kühn	Düsseldorf	2,900	62	2.1	長與	東京	3,584	71	1.99
Rössle	Kiel	540	12	2.2	加藤	京都	3,361	90	2.66
Kern	Wien	4,130	106	2.5	鈴木	〃	3,900	137	3.51
Rössle	Basel	2,445	90	3.7	矢崎，白井	新潟	1,400	21	1.5

卽歐米竝本邦に於ては孰れも1—2%の間に在りて，其の間に殆んご差異を認めざる所なり，反之原發性肝癌の頻度は兩者間に大なる逕庭ありて，本邦に於て遙かに大なること前述の如し．從て此の原因果して奈邊に在りやを考究せんには他の種の肝硬變に就て比較觀察せざるべからず．先づ此問題に入る前に肝硬變に密接なる關係を有する脾腫の態度を見れば，*Eggel* 氏は32%，*Herxheimer* 氏は42%，山根氏は60%に於て之れを合併せりと云ふ．

余は13例の Hepatom を檢せるに7例(II, III, IV, V, VI, X, XII)卽54.6%に於て脾腫を見たり．脾腫を有するこれら脾重量は何れも200g乃至450gの間に在りき．されご脾腫が果して肝硬變ニ同種の變化に基けるものなるか，或は肝臟內門脈管が肝癌のため壓迫せられ生じたる鬱血性に依るものなりやは，組織的に檢査を要す．余はこ

れがため脾臟內格子狀織維を檢せるが其の檢査數は6例(I, IV, VI, VII, IX, XIII)なりき.

輪狀萎縮性肝硬變に際して見らるゝ脾臟內格子狀織維の增殖は全く不規則なるは松井氏等の唱ふる所なり. 余の例に於ては IX, XIII の2例がこれに該當しをり, 而も IX の脾重量は 130g, XIII は 50g なりしを以て, 格子狀織維の增殖は唯脾重量のみより論ずることゝ不可能なるは勿論なり. 又鬱血性肝硬變に屬せる IV の脾臟內該織維の增殖は平等にして, 是等は稍ゝ强固ゝなりたる細織維が大部分を占め居れり. 尙鬱血性肝硬變を呈せし VI は該織維の著明なる增殖ありしが, その增殖狀態は稍ゝ不規則なりき. 又肝硬變を示しをらざりし I, VII に於ては, 該織維は可成平等に增殖せるのみならず, 又不規則なる增殖を呈せる部も有り. 卽 Hepatom に於ける脾腫は其の肝臟の硬變性變化の性質に依り一程度まで支配せらるゝも, この際鬱血は又之れに干與するものにして多くの場合は兩者の結合の結果なり.

今鬱血性肝硬變の頻度を見るに, 貴家氏は Hepatom の肝硬變 13 例中鬱血性のもの2例なりゝ云へり. 外國に於ては *Eggel* 氏は肝癌 82 例中 70 例は肝硬變を有し, その種類に關しては萎縮性 88.6 %肥大性 11.4 %なりゝ. *Herxheimer* 氏も肝硬變中に鬱血性肝硬變も極少數例に見らるゝものゝなりゝし, 其の肝癌の發生原因中に擧げ居れゞも, 其の數に就ては記載せず, 從つてこの點に就ては諸外國ゝ本邦ゝに於けるものを比較し得ざるなり. 余は上述の如く原因不明の鬱血性肝硬變2例を見たるも, 是等硬變が Hepatom の發生原因ゝなりしや又は二次的變化なりやは, 上述せる脾臟格子狀織維の增殖狀態より論ずるも, 全く決定し能はざりき. 又余の Hepatom に於てゝ硬變を有する7例中鬱血性肝硬變は, 原因の明かなりしものを合して3例なり. 是を曩に矢崎, 白井兩氏の報告せる, 當教室の剖檢材料に就き肝硬變を檢せる結果, 總肝硬變 4.93 %中鬱血性 1.07 %なるに比較すれば殆んゞ其率相似たるものあり, されゞ余の鬱血性肝硬變の頻度(3/7)は貴家氏のそれ(2/13)に比すれば稍ゝ大なるを認むるなり.

次に膽管性肝硬變ゝ Hepatom ゝの關係を見んに, 本邦に於ては肝內寄生蟲に依る肝硬變に續發せる Hepatom の存在は確定され, その一に日本住血吸蟲症に原因するものあり(草間, 貴家, 風間氏等), されゞ篦形肝蛭症は Hepatom に於ては從屬的價値を有するのみにして又併存するも膽管增殖はなきか, 又は全く輕微なりゝせり(貴家氏 1929).

然るに矢崎, 白井氏等は新潟地方は篦形肝蛭症の中等度濃厚流行地に屬し, 膽管性

肝硬變の頻度は實に1.29％(1400體中)にして他地方に比して高率なることを唱へたり．而して余のIXに於けるが如く篦形肝蛭の寄生を證明し，グ氏鞘內に於ける粗大膽管の增殖竝擴張甚だしきものあり．且間質の增殖は定型的輪狀を呈しおり，これ膽管性及萎縮性肝硬變の結合型と見るべきものにして，斯かるものゝ存在はHepatomの發生原因中日本住血吸蟲と共に興味あるものゝ如し．(篦形肝蛭の寄生を見たりしものは，Hepatom內このIXの外に尙組織的に檢し得ざりしもV，XIの2例ありき)．

其の他又余のHepatom例にして何等硬變を伴はざるもの，小兒例2例を除くも，尙1例あり，又硬變を併存すれども組織的に肝細胞の增生乃至肥大を明かにし得ざりしもの2例(IV，XIII)あり．今文獻上硬變の有無と肝癌の發生に關して最近に於ける實驗腫瘍學の教ふる所に據れば，O-amidoazotoluol 飼與に由るRatteのHepatomに於ては肝硬變を殆んど見ざりしに(佐々木，吉田氏等1933—1935)，反之Mausに於てはこれを見たりきと云ふ(吉田，川村，中澤，西山氏等)．

肝硬變の有無は動物の種類に依り如斯相違せる事實は上述民族病理學上肝癌の發生原因の一律ならざるこの間の消息を知るに有力なる根據となすを得べし．

さればHepatomの發生に關しては肝硬變を以て總べてを說明し難く，更らに他の種々なる機轉を原因とするものなるべし．

第二の發生機轉としては肝硬變に無關係なる**小兒Hepatom**に就て觀察せざるべからず．

小兒に於ける原發生肝癌の發生に就ては，山極氏は先天性基礎と見做すべき中胚葉性Teratoidのある所より肝細胞の增殖により發生するものなりと述べ，*Rosenbusch*，*Hippel*，三輪，內海，泉，木積氏等は小兒Hepatom內に屬ゝ骨，軟骨，粘液組織及上皮樣組織等の胎生期組織を見をれり．又他方に於ては小兒肝癌にして上記中胚葉性組織を證明せざりし例もあり(本田，*Mieremet*)．

又Hepatomの發生機轉に關しては成人竝小兒間には全く別種のものゝ存するを物語るに足る有力な事實は前述せる如く，多數の統計に依れば，男女略ゝ同數なることにして，成人にては女子の甚だしく少數なるに對照して意味なきに非ずとせり(*Herxheimer*)．然れども*Plaut*，*Mieremet*氏等は夫々14ヶ月及11ヶ月の小兒に於て硬變を基礎として發生せる肝癌の存在を證明せり．

余の小兒期に於ける原發性肝癌の2例を見るに，孰れも肝硬變の像なく，1例は10ヶ月の男性兒にして，腫瘍細胞は甚だしく小形にして，胎生期未分化細胞に酷似せり，卽肝細胞或は膽管上皮細胞の孰れにも移行し得る狀態に在りと謂ふを得べし．又腫瘍

組織内竝肝外轉移竈には赤血球母細胞を多量に證明す，之れ本例の腫瘍組織内には胎生期肝組織の造血機能有り，且組織の發育不全の存するは明かなり．又轉移竈に於ける上記所見より，腫瘍細胞は同時に造血作用を具備するものなりと斷定し得るなり．尙この外に先天性素因に原因するならんと惟はるゝものは心筋に見たる大形明性細胞なり．これ *Purkinjé* 氏細胞に一致するものなり，動物に在りては Glykogen を有する大なる細胞よりなり，刺戟傳導に關するものにして，人類に於てこれを見ること稀なり．要するに心筋に見たる所見は反芻動物に酷似せるなり．Ⅱ例は9歳の男兒にして，腫瘍細胞は矢張り小形にして大小不等，脂肪竝 Glykogen を有して著しく明性，核分裂像存在し異型的發育を遂げ，成人に見る定型的の Hepatom にして何等の胎生期組織と看做すべきものなかりき．

今これを文獻に依りて按ずるに，*Schlesinger* 氏は4歳の男兒に肝癌を見たり，この例に於ける腫瘍細胞は肝細胞より小にして，Mosaik 樣に密に竝び，核質に富める稍〻大なる核を有し，原形質は極僅かにして核の周圍をとりまく，又腫瘍細胞は肝組織内に浸潤性に發育を營めり．卽腫瘍細胞の性狀より云へば，余のⅠはこれに似たるものあり．又井手氏の報告例は1歳の女兒にして，腫瘍組織内に骨髓母細胞を混じをれり，其他少數例に於て骨髓樣造血組織を認むるものあれど，Ⅰの如く主腫瘍は勿論，肝外轉移竈に於ても亦腫瘍細胞の造血機能を有するは甚だ珍らしき例なりと謂ひつべし．

要するに余のⅡ例には中胚葉性組織の存在を證明し能はざりき．Ⅰ例には組織畸形乃至發育不全を認め得たりしことより，小兒に實驗せられし是等余の肝癌2例も亦先天性素因に原因せるは疑なし．

最後に其の他の肝癌の發生原因として擧ぐべきものに膽管上皮性癌に關するものあり．

肝内膽石及篦形肝蛭寄生に依る刺戟に依り增殖性膽管周圍炎を惹起し得るは明かなり，惹ては肝硬變の原因となるものにして，山極，貴家兩氏は膽管上皮性癌の發生上特に該周圍炎を重要なりとせり．先づ肝硬變と膽管上皮性癌とは如何なる關係に在りやに就て諸家の報告を見るに，山極，貴家氏等は 46.7％，*Ewing* 氏は 50％，*Herxheimer* 氏は 57％，*Eggel* 氏は 62％を擧げおれり．されば膽管上皮性癌に於ても亦硬變は先行することを屢〻なりと雖も，Hepatom に於けるが如く高率ならざるを知る．

余は5例の膽管上皮性癌中硬變を見たるは2例(XIV，XVI)にして，XIVは萎縮性，

XVI は膽管性肝硬變にて，この率 40 %なり，卽この率は諸家の報告よりも小なりき．膽管上皮性癌に於て篦形肝蛭を證明せる例には本邦に報告あるのみ．貴家氏は 27 例中 5 例にこれを見たりと云ふ．余は 5 例中 2 例 (XVI, XVII) に之れを證明せり．XVI は上述の如く膽管性肝硬變を示し居れども，XVII は膽管周圍炎を證明すれども，一般性肝硬變の像を見ること能はざりき，次に篦形肝蛭寄生と癌腫發生の割合を見るに，本邦に報告あるのみにして，桂田氏は 56 例の篦形肝蛭寄生屍中唯 1 例卽約 1.8 %，井上氏は 1.3 % (3/234) なりと云ふ．余の檢索せる結果は 202 例の篦形肝蛭寄生屍中 (總屍數 2049 體に對し) 2 例に癌腫發生を見，卽約 1 %なり．從て篦形肝蛭寄生より癌腫發生を見る割合は甚だ小なるものなり．最後に膽石と膽管上皮性癌との關係を見るに，*Eggel* 氏は 116 例中 14 例，貴家氏は 27 例中 8 例にこれを證明せり．余の例に於ては 5 例中 2 例 (XV, XVIII) なり．XVIII に於ては腫瘍組織內にも膽石を認めたり．膽石形成竝癌腫發生との時期に就ては論じ難し，果して癌腫發生後膽石が形成せられしものなりや否やは，測り知るべからざるが故に，膽石が癌腫發生の直接の原因たりしことは斷定し得ず．されど XVIII の如く癌腫發生部位に膽石を見たることより，少なくもこれが癌腫發生に干與せざるを否定し能はざるべし．

第七章　結　論

1)　過去 25 年間の當病理學教室に於ける總剖檢屍數 2165 體に對し原發性肝癌は 18 例ありて 0.83 %に當る．尙原發性肝癌，膽囊癌竝總輸膽管癌との比は夫々 18 : 16 : 7 となる．又續發性のものを含む全肝癌中原發性のものは 21.2 %なり．更らに 18 例中膽管上皮性癌は 27.78 %に當れり．

2)　「ヘパトーム」は 13 例にして形態學的分類に於ては その 69.23 %は結節狀，23.07 %は混塊狀，7.69 %は瀰蔓性なりき．5 例の膽管上皮性癌は總べて混塊狀を呈し單發せり．

3)　膽管上皮性癌に於ける肝平均重量は 1250g にして肝臟の腫大を見ざりしも，「ヘパトーム」の其れは 2532.08±181.08g にして最大のもの 3600g に腫大せり．

4)　膽管上皮性癌に於ける肝臟の橫隔膜との癒著狀態は 高度なりしも，「ヘパトーム」に於ても亦癒著は稀ならず．

5)　小兒「ヘパトーム」の轉移形成は殊に廣範なり，成人に於ても「ヘパトーム」の肝外轉移は從來考へられしが如く稀有のものに非らず，唯他の癌腫に比して大さ小にして組織的に證明し得る程度のもの多きの差あるのみ．

膽管上皮性癌に於ては周知の如く高度の轉移形成を證明し得たり．部位的淋巴腺轉移は80％，肋膜播種結節は60％に見たりき．

6) 「ヘパトーム」に於ては10歲以下に2例，40歲より60歲の間に11例あり．反之膽管上皮性癌に於ては30歲より60歲の間に見られたりき．又性別に就ては男子は女子より遙かに多く，兩種癌腫に於て，其の率は略〻相等しく「ヘパトーム」は男子76.93％，膽管上皮性癌は男子80％なりき．

7) 腹水の證明せられしは18例中15例にして83.3％，黄疸は7例，38.9％なり．腹水ミ同時に蛋白尿のありしは「ヘパトーム」のみに證明せり．

8) 第VII例に於ては肺臟轉移結節竝內の毛細管內被細胞內に膽汁色素を證明せり．この事實竝その他の點より網狀織內被細胞は病的の場合に於ても「ビリルビン」形成に關して重要なる役割を演ずるものなるを確め得たり．

9) 「ヘパトーム」腫瘍細胞內脂肪竝肝細胞內脂肪の消長は略〻平行せるもの〻如し．是等腫瘍細胞內脂肪の性狀に關しては，主ミして中性脂肪にして，「コレステリン・エステル」は44％(4/9)の割合に混じ居り，又少量の「リポイド」を含有せり．壞死竝には相當量の「コレステリン・エステル」の混在せるを見たりき．反之膽管上皮性癌に於ける腫瘍細胞內脂肪の出現は「ヘパトーム」に比し遙かに少量にして，この大部分は「リポイド」なりき．

肝組織內クパー氏星芒細胞內脂肪は兩種癌腫を通じ46.15％(6/13)に見られ，又間質脂肪には「コレステリン・エステル」の出現屢〻なりき．

10) 格子狀纖維の發育は「ヘパトーム」は膽管上皮性癌に比し良好なれごも，肝組織に於ける該纖維に比し著明なる增殖を見ざりき．

11) 第VI例に觀たるが如き小初期結節に於て移行像を認めたり，この點より余は「ヘパトーム」の多中心性發生を信ず．

12) 膽管上皮性癌5例中，この癌腫發生上從來原因ミして擧げらる〻膽石2例，筬形肝蛭寄生2例を證明せり．

「ヘパトーム」の發生に就ては小兒に見らる〻ものは先天性素因に基くものならんも，成人に於けるものは屢〻肝硬變を合併し，これが大多數の「ヘパトーム」に於て原因ミなるは勿論なり．されご硬變を有せる例にも組織的には肝細胞の肥大乃至增生を見ざるもの尙少數例あるのみならず，更らに全然肝硬變を缺如せる例を證明し得るを見れば，「ヘパトーム」の發生には硬變以外の他の發生機轉の存在を信ぜざるべからず．

擱筆に臨み謹んで恩師川村教授の御指導竝に御校閲に對して深謝す．

文　献

1) *Adelheim, R.*, Frankf. Zeitschr. f. Pathol., Bd. 14, 1913. 2) *Adler. L.*, Beitr. z. pathol. Anat. u. z. allg. Pathol., Bd. 35, 1904. 3) *Blumberg*, Frank. Zeitschr. f. Pathol., Bd. 10, 1912. 4) *Castle*, Surg. Gynecol. & Obster., Vol. 18, 1914. 5) *Counceller & McIndoe*, Arch. of Internal Med., Vol. 37, 1926. 6) *Eggel*, Beitr. z. pathol. Anat. u. z. allg. Pathol., Bd. 30, 1901. 7) *Culpepper, A. L.*, Ame. J. of. Canc., Vol. 21, 1934. 8) *Ewing*, Neoplastic Deseases, 2nd ed., London, 1922. 9) *Goldzieher* u. *v. Bókay*, V. A., Bd. 203, 1911. 10) *Griffith C.*, Ame. J. of the Med. Sciences, Vol. 155, 1918. 11) *Hansemann*, Berl. klin. Wochenschr., 1890. 12) *Herxheimer*, Zentralbl. f. allg. Pathol. u. pathol. Anat., Bd. 17, 1906. 13) 服部, 北越醫學會雜誌, 第199號, 大正3年. 14) *Hippel, , V.*, V. A., Bd. 291, 1910. 15) 本田, 癌, 第5年, 明治44年. 16) *Huguenin, B.*, Zentralbl. f. allg. Pathol. u. pathol. Anat., Bd. 22, 1911. 17) 井手, 兒科雜誌, 183號, 大正4年. 18) 泉, Arch. f. klin. Chirurg., Bd. 100, 1913. 19) 桂田, 東京醫學會雜誌, 第11卷, 明治30年. 20) 風間, 東京醫事新誌, 第2294竝2295號, 大正11年. 21) 貴家, 癌, 第2年及3年, 明治41年及42年. 癌, 第23年, 昭和4年. 22) 木積, 日本病理學會會誌, 第5年, 大正4年. 23) *Kretz R.*, *Lubarsch Ostertags* Ergebn., 1902, 8. Jahrg. 24) 草間, 癌, 第一年, 明治40年. 25) 楠本, 北越醫學會雜誌, 51年, 7號, 昭和11年 26) *Lissauer*, V. A., Bd. 202, 1910. 27) *Landsteiner*, Zit. nach *Lubarsch*. 28) *Lubarsch*, Handb. d. spez. pathol. Anat. u. Histol., Bd. 5. Tl. 1, *G. Herxheimer*. 29) 松井, 癌, 第7年, 大正2年. 日本病理學會會誌, 第3卷, 大正2年. 30) *Mieremet*, Zeitschr. f. Krebsforsch., Bd. 17, 1920. 31) *Mirolubow*, V. A., Bd. 209, 1912. 32) 三浦, 東京醫學會雜誌, 第2卷, 明治21年. 33) 三輪, 內海, 兒科雜誌, 119號, 明治43年. 34) 室, 朝鮮醫學會雜誌, 22卷, 昭和7年. 35) 長與, 東大紀要, 第9卷, 1911. 癌, 第26卷, 昭和7年. 36) 中村, 土橋, 癌, 第1年, 明治40年. 37) 新島, 京都醫學會雜誌, 22年, 大正14年, 38) 仁藤, 東京醫學會雜誌, 24卷, 明治43年. 39) 西山, 癌, 第29卷, 昭和10年. 40) *Nobiling, H.*, Zeitschr. f. Krebsforsch., Bd. 10, 1911. 41) 岡田, 十全會雜誌, 32卷, 昭和2年. 42) 岡崎, 成醫會月報, 395號, 大正4年. 43) *Plaut*, Arch. f. Kinderheilk., Bd. 43, 1906. 44) *Prym*, Frankf. Zeitschr. f. Pathol., Bd. 10, 1912. 45) *Rénon, Geraudel* et *Monier Vinard*, Zentralbl. f. allg. Pathol., Bd. 22, 1911. 46) *Ribbert. H.*, Deutsch. med. Wochenschr., 1909 II. 47) *Rosenbusch*, V. A., Bd. 261, 1926. 48) *Saltykow*, Verhandl. d. dtsch. pathol. Ges., 15. Tag., 1912. 49) 佐々木, 吉田, 日本病理學會會誌, 24卷, 昭和9年. V. A., Bd. 295, 1935. 50) *Schlesinger, E.*, Jahrb. f. Kinderheilk., Bd. 55, 1902. 51) *v. Siegenbeek, Heukelom*, Beitr. z. pathol. Anat. u. allg. Pathol., Bd. 16, 1894. 52) *Stromeyer, K.*, Zentralbl. f. allg. Pathol. u. pathol. Anat., Bd. 23, 1912. 53) 高泉, 癌, 第16年, 大正11年. 54) 瀧澤, Zentralbl. f. allg. Pathol. u. pathol. Anat., Bd. 61, 1934. 55) 田中, 癌, 第28卷, 昭和9年. 56) 田中(修), 北越醫學會雜誌, 第40年, 大正14年. 57) 塚本, 北越醫學會雜誌, 第42年, 昭和2年. 58) *Wegelin*, V. A., Bd. 179, 1905. 59) *Winternitz, M. C.*, V. A., Bd. 209, 1912. 60) 山極, V. A., Bd. 206, 1911. 癌, 第4年, 明治43年. 61) 山根, 日本病理學會會誌, 第8年, 大正7年. 62) 矢崎, 白井, 北越醫學會雜誌, 第48年, 昭和8年.

Auszug

Über primäre Leberkrebse

Von

Shigeo Hudimaki

(Tafeln XXX—XXXI)

(Aus dem Pathologischen Institut der Niigata Med. Fakultät. Vorstand: Prof. Dr. *R. Kawamura*)

(Eingegangen am 14. August 1936)

Es wurde vor kurzem das Rattenhepatom durch Fütterung mit O-amidoazotoluol von *Sasaki* und *Yoshida* erzeugt, was zur Aufklärung des Wesens dieser Krankheit einen wichtigen Beitrag gibt.

Neben dieser interessanten experimentellen Untersuchung ist es noch immerhin notwendig, an den verschiedenen Lokalen, besonders in Rücksicht auf die Verschiedenheit der geographischen Verteilung, über die Pathologie, insbesondere Pathogenese der primären Leberkrebse eine eingehende Forschung anzustellen, obwohl schon eine grosse Zahl von Arbeiten darüber veröffentlicht worden ist.

1) Am hiesigen Institut wurden von Jahre 1911 bis 1935, 2165 Leichen seziert, darunter hat der Verfasser das Leberkarzinom in 18 Fällen, d. h. 0.83% der Sektionsfälle gefunden. Diese Zahl ist sechs bis sieben mal grösser als in den ausländischen Statistiken von 0.12% (*Lubarsch*) oder 0.14% (*Counceller, McIndoe*). Diese Tatsache soll auch dadurch unterstützt werden, dass in unseren Sektionsfällen die primären unter den ganzen Leberkrebsen 21.2% ausmachen, in den Arbeiten der ausländischen Forscher nur 1.5 bis 5%. Das Häufigkeitsverhältnis von Krebsen der Leber, Gallenblase und der grösseren Gallengänge in unseren Fällen ist 18 : 16 : 7, doch kommen in Europa Gallenblasenkrebse ca. zwei bis zehn mal häufiger als primäre Leberkrebse vor. Meine 18 Fälle von primärem Leberkrebs wurden der Entstehung nach in zwei Gruppen eingeteilt: Leberzellenkrebs, Hepatom, von 13 Fällen und Gallengangskrebs, Cholangiom, von 5.

2) Was die Metastasenbildung beim Hepatom anbelangt, wurde sie ausser intrahepatischer Geschwulstthrombose der V. portae und V. cava inferior, bei zwei Kinderfällen (Fall I und II) in den periportalen, retroperitonealen, paratrachealen Lymphdrüsen, Lunge, Niere, Pancreas und Nebenniere und ferner beim Fall XIII in einer periportalen Lymphdrüse eine

haematogen eingeschleppte Geschwulstzellengruppe wahrgenommen. Danach ist die extrahepatische Metastasenbildung beim Hepatom im Gegensatz zur allgemeinen Annahme kein so seltenes Ereignis.

Beim Cholangiom waren die Metastasen, wie bekanntlich, viel ausgedehnter, und sie geschahen hauptsächlich auf dem Lymphwege; sie waren in 80% in periportaler Lymphdrüse, in 60% Pleuraldissemination und in 40% Peritonealdissemination und krebsige Verdickung des Zwerchfells.

3) Unter sämtlichen Fällen von Hepatom wurden morphologisch 9 in knotiger Form, 3 in massiver und nur einer in diffuser Form gefunden, während Cholangiom in allen Fällen massive Form darstellte.

4) Bei histologischer Untersuchung der 9 Fälle von Hepatom waren die Geschwulstzellen in 6 Fällen basophil, in 2 Fällen acidophil gefärbt und baso- und acidophil gefärbte fanden sich nur in einem Fall beimischt.

5) In allen Hepatomfällen bestand das Stroma aus Blutkapillaren, dagegen beim Cholangiom war das Geschwulstgewebe adenokarzinomatös beschaffen, und zwar bestanden unter 5 Fällen 2 aus Drüsenzellen und 3 aus Zylinderzellen.

6) Luminabildungen der Geschwulstalveolen beim Hepatom wurden in 5 unter 10 Fällen nachgewiesen; ein Teil davon entstand aus dilatierten Gallenkapillaren, was mit Rosetten nach *Yamagiwa* ganz übereinstimmt, ein anderer war als durch Nekrose entstandene Erweichungscyste zu betrachten.

7) Gallenpigmente liessen sich in den Hepatomzellen in 3 unter 10 Fällen als grüne bis gelbbraune Körner oder Zylinder nachweisen, die im gesunden Lebergewebe dieser Fälle nicht wahrgenommen wurden. Umgekehrt fanden sich einige Fälle, in deren Geschwulstzellen Gallenpigment nirgends beobachtet wurde trotz des deutlichen Ikterus der Leber. Daher können die Hepatomzellen im gesunden Zustand genügend befähigt sein, Galle zu bilden, abgesehen davon, dass degenerierte Geschwulstzellen natürlicherweise von Galle imbibiert werden können. Ferner konnte der Verfasser bei einem Hepatomfall Gallenpigmente in *Kupffer*schen Sternzellen im metastatischen Knoten der Lunge finden; der Bilirubingehalt des Blutes in diesem Fall war 8 nach *Meulengracht*, welches innerhalb der physiologischen Grenze liegt und es wurde dabei noch kein Ikterus im Lebergewebe nachgewiesen. Hiernach kann man wohl schliessen, dass sich die *Kupffer*schen Sternzellen auch im Tumorgewebe an der Bilirubinbildung beteiligen.

8) In 9 Fällen von Hepatom und in 4 von Cholangiom wurde auf Fette untersucht.

Die Hepatomzellen waren im allgemeinen stark verfettet, doch gab es

einige, welche zwar nach der alten Fettfärbungsmethode keine, aber bei der Methode nach *Kawamura-Yasaki* eine deutliche Verfettung aufwiesen. Der Natur nach waren die Fette hauptsächlich neutrale Fette, denen noch eine grosse Menge von Lipoid und in 44.4% der Fälle Cholesterinester beimischt war. Dagegen verhielt sich das Cholangiom verschieden. In der Regel waren die Geschwulstzellen viel geringer verfettet als beim Hepatom und die Fette bestanden hauptsächlich aus Lipoiden.

Die Kerne der Hepatomzellen zeigten ab und zu eine starke Verfettung unabhängig vom Fettgehalt ihres Protoplasmas. Dieses Kernfett konnte aber beim Cholangiom niemals beobachtet werden.

Cholesterinester traten in relativ grosser Menge in Lumina des Adenokarzinoms beim Cholangiom und im Interstitium in beiden Krebsarten auf. Sie wurden auch an nekrotischen Stellen des Hepatomgewebes in reichlicher Menge bestätigt.

Bezüglich des Mengenverhältnisses der Fette zwischen Hepatom- und Leberzellen besteht in der Regel ein Parallelismus, nämlich im Fall VIII und X wenig, dagegen in den Fällen II, IV, VII und XIII reichlich in beiden. Davon machte Fall I eine Ausnahme, indem trotz der Fettleber die Verfettung der Hepatomzellen nur angedeutet vorhanden war. Über die Herkunft der Fette sind sie nach den Resultaten des Verfassers exogener Natur, sodass Fettinfiltration wie in gewöhnlichem Lebergewebe angenommen werden kann.

9) In den nach *Carnoy* fixierten Hepatomfällen wurden bei 4 Glykogenkörner nachgewiesen, aber in keinem Fall von Cholangiom. Ferner konnte der Verfasser sie in 2 Fällen darunter in Kernen der stark verfetteten Geschwulstzellen auffindig machen. Es soll hier ein inniger Zusammenhang zwischen beiden angenommen werden.

10) Die Gitterfasern waren an der Kapillarenwand der Alveolen des Hepatoms jedesmal relativ gut entwickelt und drangen in 5 Fällen als umspinnende Fasern zwischen die einzelnen Zellen hinein. Doch waren sie nicht so gut entwickelt wie die radiären und umspinnenden Fasern des Lebergewebes. Beim Cholangiom fanden sich die Gitterfasern im Interstitium in grosser Menge, aber nicht zwischen den Geschwulstzellen.

11) Primäre Leberkrebse, insbesondere Hepatome sind bekanntlich sehr häufig mit Leberzirrhose kombiniert. Dass ihnen eine Leberzirrhose vorangegangen ist, konnte der Verfasser bei 3 Fällen bestätigen, welche klinisch als Leberzirrhose behandelt worden waren, und bei der Leichenöffnung ausser Leberzirrhose gleichzeitige Krebsbildung aufwiesen. Und zwar fanden sich

in einem Fall VI mehrere kleine Hepatomknoten, in deren einem allmähliches Übergehen der Leberzellen ins Krebsgewebe beobachtet wurde, dessen hyperplasierte Leberazini durch Chromatinzunahme und Vergrösserung der Kerne ausgezeichnet waren. Dieser Fall gehörte der Stauungszirrhose an. Da die Geschwulstknoten sich fast alle in gleichem Entwicklungszustand vorfanden und keine Unterscheidung von Haupt- und Nebenknoten gemacht werden konnte, sollten sie multizentrisch an mehreren Stellen entstanden sein.

Der Verfasser beobachtete Leberzirrhose in 76.9% unter 13 Hepatomfällen.

Nach der Art der Zirrhose wurde *Laennec*sche atrophische Leberzirrhose in 3, Stauungszirrhose in 3 und biliär- atrophisch kombinierte Form in einem Fall von 3 Fällen festgestellt, in welchem infolge Einnistens der Leberdistoma, ausser annulärer Verdickung der *Glisson*schen Scheide, eine starke fibröse Wucherung der Gallengänge nachweisbar war. Dieser Fall spricht dafür, dass in der Hepatomgenesis Distomiasis, ferner Schistosomiasis jap., berücksichtigt werden muss.

Was die Häufigkeit der atrophischen Leberzirrhose auf dem Sektionstisch anbelangt, gibt es zwischen unserem Lande und Europa keinen grossen Unterschied, nämlich zwischen 1 bis 2%. Woher aber kommt das Überwiegen des Hepatoms in Japan im Gegensatz zu Europa? Es müssen noch andere ätiologische Umstände als Leberzirrhose in Betracht kommen, um Hepatom hervorzurufen. Es gab in der Tat unter meinen Hepatomfällen einige, in denen trotz der Leberzirrhose weder Hyperplasie noch Hypertrophie der Leberzellen vorhanden war. Ferner waren 3 Hepatomfälle ganz frei von zirrhotischer Veränderung, 2 davon waren kleine Kinder und so sollte dabei die Hepatombildung auf embryonale Anlage zurückzuführen sein.

Zuletzt konnte der Verfasser beim Cholangiom Gallensteine in 2, Leberdistoma in 2 Fällen bestätigen, was für die Krebsbildung eine ätiologische Bedeutung haben dürfte. (*Autoreferat.*)

Erklärung der Abbildungen

Abb. I. Metastatische Hepatomzellengruppe (H) in einer periportalen Lymphdrüse, Fall XIII.
Abb. II. Becherzellen (B) beim Cholangiom, Fall XIV.
Abb. III. Cholangiom, Fall XVI.
Abb. IV. Trabekulärer Typus von Hepatom, Fall XIII.
Abb. V. Rosettenbildung (R) beim Hepatom, Fall IX.
Abb. VI. Luminabildung (L) im medullären Typus von Hepatom, Fall II.
Abb. VII. Adenomatöses Gebilde (A) im Lebergewebe beim Hepatom, Fall IX.
Abb. VIII. Übergangsbild zum beginnenden Hepatomknoten, Fall VI.

Abb. I

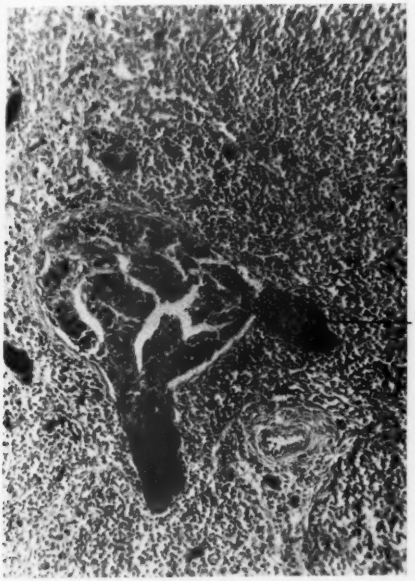


Abb. II

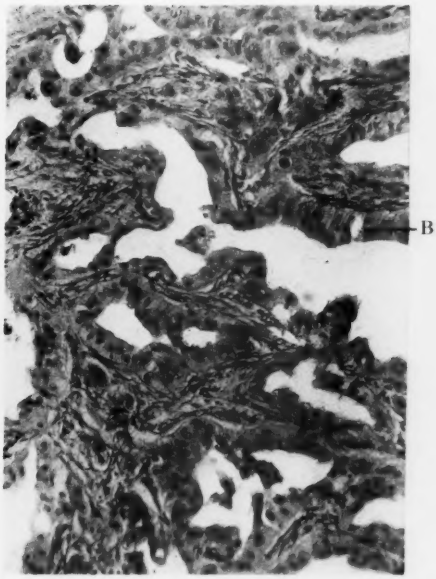


Abb. III

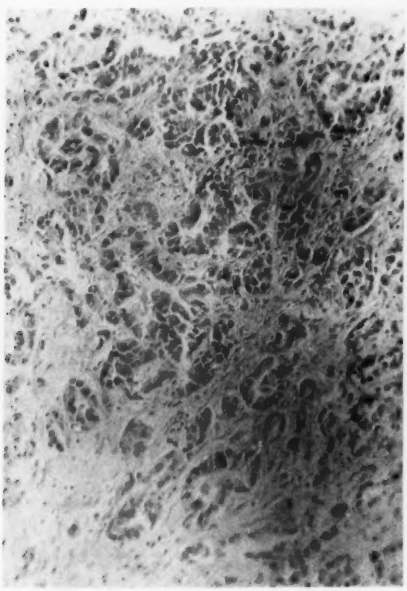
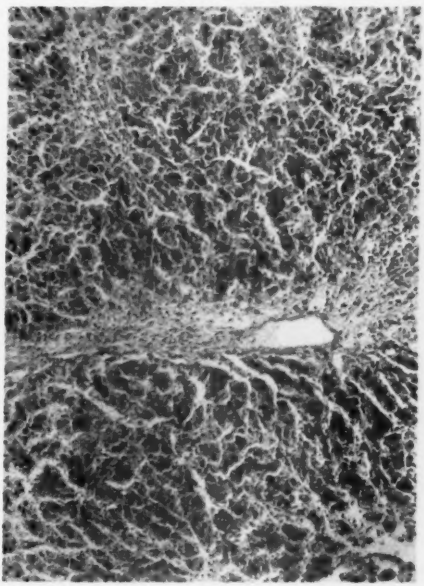


Abb. IV



Shigeo Hudimaki: Über primäre Leberkrebse

Abb. V

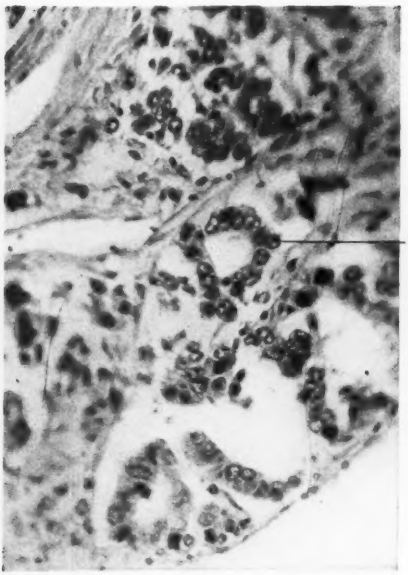


Abb. VI

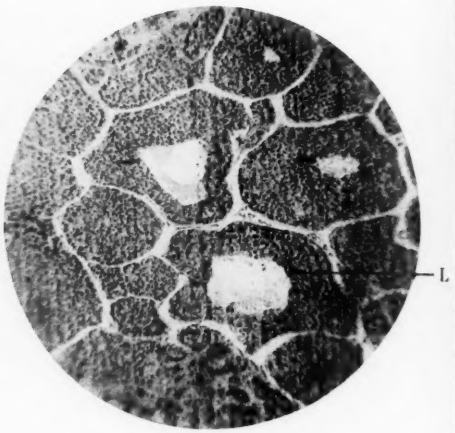


Abb. VII

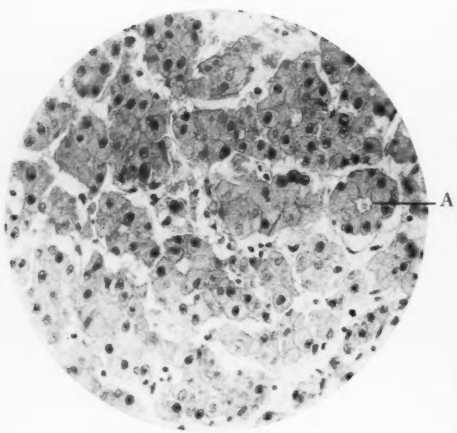
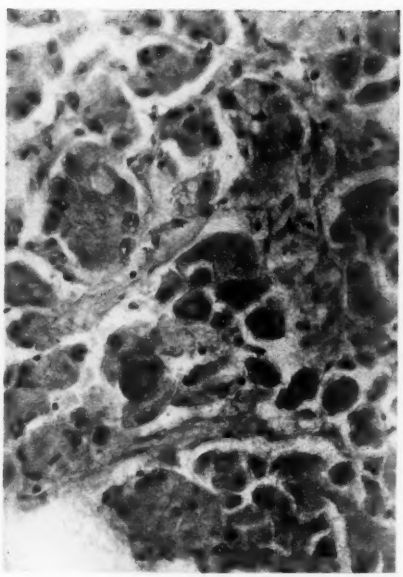


Abb. VIII



綜　說　REVIEW

癌腫の惡性度について

緒方知三郎

癌腫の惡性度についてゝいふ演題を掲げて置きましたが，私はこの席で述べようゝ思つてゐます内容は，米國で histological grading of malignancy (惡性の組織學的度分け)ゝ稱へてゐる事項に限られてゐるこゝを豫め御承知願ひます．

本問題は既に研究し論じ盡された過去に屬するゝいつても過言でない事項でありますが，我國に於ては一般にあまり注意せられずに過ぎ去つてしまつてゐる樣に考へますので，この問題に參與した各研究者が何ういふ風に癌腫の惡性度を組織學的に度分けしたかゝいふこの大體を知つて置くこゝは，今後の研究に大に參考になるこゝゝ思ひますから，調べました所を簡單に御話致し，それが終りましてから幻燈を用ひて各研究者の度分けした癌腫の組織像を御覽に入れるこゝに致します．

この問題は今から約 40 年近く以前に行はれた獨逸の *v. Hansemann* の研究に基を發するものであります．*v. Hansemann* は西歷 1890 年 Virchow's Archiv 第 119 卷に Über asymmetrische Zellteilung in Epithelkrebsen und deren biologische Bedeutung なる一論文を公にし，その中に彼の有名な Anaplasie の學說を述べました．この學說はそれから 3 年後に單行本ゝして刊行せられた Studien über die Spezifität, den Altruismus und die Anaplasie der Zellen (1893) ゝいふ彼れの著書の中に一層明かに記述せられてゐます．

彼れの Anaplasie に關する學說の梗概は次の通りであります．彼れは生理的の細胞が惡性の腫瘍となる際に現はれるその生物學的の性狀の變化を Anaplasie と呼び，そしてこの性狀の變化は細胞が分化する能力を失つて，それよりも未分化な未熟な發育狀態に退化すると共にその發育の獨立性を獲得するからであると解釋しました．Anaplasie といふ術語にはこの意が含まれてゐるのでありまして，ana- (ἀνά-) といふ接頭語は一般には「上に昇る」とか，「再び繰りかへす」といふことを意味するが，その他に「後に退く」といふ意味があるので，この稀に用ひられる退くといふ意味でこれを用ひたものであります．それでありますから Anaplasie は「退形成」と譯せらる可き術語であるのであります．上述の論文では前に申した通りに彼れは分化の退行といふ點を强調したが，後には生理的には認められない新しい細胞の種類に變ずるのであるといふ風に說が變つて行つたので，Anaplasie といふ術語の現はす病變の內容が異なるものとなり，從つて彼

れの學說の特徵は多少失はるゝに至つたのであります．そして彼れは又始めからこの Anaplasie の起る主因を細胞核の非對稱性分剖に求めたのでありました．非對稱性分剖に際して細胞核が大小の大さを異にした2個の核に分れる場合に，細胞の性狀を特色づける可き核の特殊の成分が小さな核を持つ細胞の方に移り大きな核を持つ細胞はこれを含まないことになるので，その結果生理的の細胞は分化の退行を起して終に癌細胞となると說明しました．

然しその後非對稱分剖は一般に組織の增殖の起る場合にも認められ，必ずしも癌腫の發生に際してのみ現はれるものでないことが明になつたので，彼も後年にはその主張を遠慮するようになりました．然し彼れの Anaplasie 學說の根本的の考へ方は今日でも一般に認められてゐるのであります．

茲に序に *v. Hansemann* の Anaplasie 學說と殆んど同じ內容をもつ *Beneke* の Kataplasie 學說を述べることは無用ではないと思ひます．*Beneke* は *v. Hansemann* より 10 年遲れて西曆 1900 年に癌腫發生の機轉を Kataplasie と稱へました．kata-(κατά)は「下に降る」ことを意味する接頭語であるから，この術語は「降形成」と譯さる可きものであります．

彼れはこの術語を以て癌腫の發生に際して生理的の細胞が本來具へてゐた特異の機能を全く失ふか又その減退を來すと同時に成長のエネルギーを獲得することを意味せしめたのであります．生理的な細胞の働きを失つて下等な細胞になるといふのであります．*v. Hansemann* の Anaplasie と異なるところは腫瘍細胞が活潑なる發育を現はすのは胎生學的に分化したのと正反對に退化して若い未熟な狀態になるといふのではなく，全く他の新しい方向へと下降するといふ點にあります．然し前にも述べた如く *v. Hansemann* は後に彼の主張を改めて必ずしも逆行の意味にあらず新しい細胞種への變化といふ風に說いてゐるので，Anaplasie と Kataplasie は同じ內容を持つ術語となつてしまつたのであります．それで今日私共は兩者を同意のものとして使用してゐる次第であります．

上に述べ來つた通りの次第で，*v. Hansemann* は Anaplasie を以て生理的の細胞が惡性腫瘍に變化する時に起る生物學的性狀の異常を意味したのでありますが，彼れの立場が病理解剖學であつたために彼れは便宜上屢〻これを以てその際認められる形態學的の變化を呼ぶようになつたのであります．而してこの意味に於ける形態學的組織學的の Anaplasie の程度と癌腫の惡性度との關係に就ては，彼れは始めのうちはそれが正比例して增減するといふことについて斷定的な結論を述べることを躊躇してゐる風に見えましたが，西曆 1897 年に至つて彼れの著書 Die mikroskopische Diagnose der bösartigen Geschwülste (1897) に於てその間に一定の關係の存在することを認め Anaplasie の程度によつて腫瘍の惡性度を大體に於て判斷し得るものであると主張するに至つたものであります．彼れは癌腫の組織像によつて Anaplasie の程度を

輕度，中等度，强度の三程度に分けました．無論これは彼れの學說によつて明かなる如く生理的の上皮細胞から分化を失ふ程度，卽ち退化の程度を以てこれを度分けしたのであります．例へば扁平上皮癌に於ては生理的の扁平上皮に見られる角化（分化の現はれ）が不明ㇾなる程度，圓柱上皮癌に於ては圓柱上皮の形態が不明瞭ㇾなり終には管腔を現はさざるに至る程度を以て Anaplasie の度分けをしたのであります．

この *v. Hansemann* の Anaplasie ㇾ惡性度ㇾの關係についての考へはその本國の獨逸は勿論歐洲各國では臨牀家の注意を惹かず，これに關する少數の文獻が現はれた位で過ぎ去つてしまつたのでしたが，約四分の一世紀以上もたつた後に，米國に於て再びこの問題がむしかへされる事になつたのであります．西歷 1920 年米國ミネソタ州ロチェスター市のメイヨー病院の臨牀病理學者 *Broders* はその病院で外科的に切除せられた口脣癌の多數例について，組織學的檢査を行つて，その組織像ㇾ手術の豫後ㇾを比較考察して，*v. Hansemann* ㇾ全く同じ樣に上皮の退化の進むㇾ共に惡性度の增加するㇾを明にしたのであります．私は先年東大から歐米に出張を命ぜられて各國醫學の視察に參りました節，同氏に面會して親しくこの研究について說明してもらつたのでありましたが，*v. Hansemann* の Anaplasie その儘の考へ方であるにも拘はらず，*v. Hansemann* のㇾについて彼は一言もふれませんでした．又彼の論文を讀んで見ましたが，これ亦そのㇾについては全く述べてゐないのであります．私は彼のこの問題に對する功績は他の人が棄てゝ顧みなかつた *v. Hansemann* の Anaplasie に關する考へ方を多數の臨牀例について確證したといふ點に在るㇾ考へてゐるのであります．

Broders は癌腫をその Anaplasie の程度（前にも申しました通り彼れ自身は Anaplasie ㇾは云はず，上皮細胞の分化，未分化の程度ㇾいつてゐます）に從つて四つの階級に分けてゐます．この度分けのやり方は腫瘍の色々の部分から組織標本を作つて，これを全部檢鏡した上で，その全癌腫組織の癌細胞の中で分化したもの（扁平上皮癌では角化，圓柱上皮癌では腺樣構造が著明なもの）ㇾ未分化のもの（扁平上皮癌では角化の傾向なきもの，圓柱上皮癌では腺樣構造の不明のもの）ㇾの數の割合を目測で決定するのであります．そして彼は始めの中（1920）は次の如き標準で度分けしてゐたのであります．彼れの第1度ㇾいふのは分化したものが全癌細胞の4分の3を占め，未分化のものが僅かに4分の1に過ぎないものをいひ，第2度ㇾは分化2分の1，未分化2分の1で兩者互に相半ばしてゐるもの，第3度は第1度ㇾ反對に未分化のものが4分の3で，分化したものが4分の1に過ぎないもの，第4度ㇾは全部の癌細胞が未分

化のものばかりで，分化したものは見出せないものさいふ風に分けてゐたのであります．この度分けの標準を以て實際に臨むさ *Broders* 自身でも，何れに入れてよいかわからぬ中間の程度のものがあるさ見えて，後(1924)にはこの度分のやり方を次の通りに改めてゐます．第1度は分化したもの100—75%，未分化のもの0—25%，第2度は分化したもの 75—50%，未分化のもの25—50%，第3度は分化したもの 50—25%，未分化のもの 50—75%，第4度は分化したもの 25—0%，未分化のもの 75—100%さ大分ゆさりをつけた方法にはなつてゐますが，根が目測でありますから，同じ研究者が時を置いて同じ材料についてこの標準に從つて度分けをした場合に第1回目に第2度さ定めたものが，第2回目には第3度さなり，又これさ反對のこさも可能でありまして，この度分けは決して尺度で物をはかる樣に正確に行くものでないこさは，この度分けを一度試みたものが直ちに氣づく事であります．然し彼れは兎に角この標準に從つて度分けをした上で，その各例の豫後さ對照して見るさ大體に於て第1度，第2度，第3度，第4度さ度の進むに從つて豫後が悪いさいふこさを確めたのであります．前に申しました通りこの事實は先づ口唇癌について認められたのでありますが，その後この問題が先づ米國に於て盛に討議せられ，彼の他に多數の研究者が續出して他の部位の癌腫についても亦同樣な關係が成立するこさを認めた學者が多くあるのであります．今次に掲げた表を御覽になつてこの一般を御理解願ひたいさ存じます．

番號	年代	研究者	研究材料	度分けの數	成績
1	1893—7	*Hansemann*	扁平上皮癌，腺癌	3	+
2	1907	*Halstead*	乳癌	6	+
3	1913	*Salomon*	乳癌	2 5	+ +
4	1914	*Lindenberg*	乳癌	3	+
5	1920—21	*Broders*	口脣癌	4	+
6	1921	*Broders*	皮膚癌	4	+
7	1921	*Boss*	乳癌	5	+
8	1921	*Hoffmann*	乳癌	3	+
9	1922	*MacCarty*	乳癌	defensive factors	+
10	1922	*Feist, Bauer*	乳癌	3	+
11	1922	*Broders*	泌尿生殖器の癌	4	+
12	1923	*Martzloff*	子宮腟部癌	3	+
13	1923	*Mahle*	子宮體部癌	4	+
14	1925	*Greenough*	乳癌	4	−
15	1925	*Greenough*	乳癌	3	+
16	1925	*Heuper, Schmitz*	乳癌	histological malignogram	+

17	1925	*Crenshaw* (*Broders* 指導)	膀胱癌	4	+
18	1925	*Broders*	膽嚢癌, 口唇癌, 胃腸癌	4	+
19	1927	*White*	乳　癌	3	+
20	1927	*Delbet, Mandars*	乳　癌	5	+(或る程度まで)
21	1927	*Plaut*	乳　癌		−
22	1927	*Rankin, Broders*	直腸癌	4	+
23	1927	*Dahl, Inversen*	乳　癌	4	+
24	1927	*Broders*	舌　癌	4	+
25	1928	*Broders, Vinson*	食道癌	4	+
26	1928	*Lee, Stubenbord* (*Ewing*)	乳　癌	3	+
27	1928	*Partey, Scharff*	乳　癌	3	+
28	1928	*Flothow*	乳癌, 子宮癌	defensive factors	+
29	1929	*Reimann*	乳　癌	3	−
30	1929	*Smith, Bartlett*	乳　癌	3	+
31	1930	*Leroux, Perrot*	乳　癌	2	+
32	1931	*Bertrand, de Nagy*	乳　癌	2	−
33	1831	*Balfour* (*Broders* 指導)	胃　癌	4	+
34	1931	*Pemberton, Fricke*	甲狀腺癌	4	+
35	1931	*New*	喉頭癌	4	+
36	1631	*Vinson*	氣管枝癌	4	+
37	1931	*Warren*	子宮頸部癌	3	+
38	1932	*Mureau, Lambert*	乳　癌	2	+
39	1933	*Haagensen*	乳　癌	3	+
40	1933	*Ngai* (*Broders* 指導)	陰莖癌	4	+
41	1933	*Stewart*	子宮體部癌, 甲狀腺癌	4	+
42	1933	*Watson*	食道癌	3	+

この表を御覽になつて御氣づきになるこ思ひますが *v. Hansemann* から *Broders* に至る間に *Halstead, Salomon, Lindenberg* 等の研究がありますが, これは唯癌の組織學的構造に從つて任意に分類してその豫後に良悪あるを述べてゐるもので, *Hansemann* の眞の流をくんだ Anaplasie の考へ方から出發したものでない上にその材料も少數であるので殆んご取りあげる價値はないのでありますから, 前に申しあげた通り實際には *v. Hansemann* の研究から *Broders* に飛んで考へて少しも差支えないのであります. 御覽の通り *Broders* はその後も引き續いてこの問題の研究に從事してゐまして, 彼れの指導によつて作られた業績も多數あるのであります. その功績は充分に認めてやつてよいのであります.

それから表に現はしてあります通り各研究者によつて度分けの數が異つてゐるのであります. 前に述べましたやうに始め *v. Hansemann* は輕度, 中等度, 强度の Anaplasie に分けたのでありますが, *Broders* はこれを第1度, 第2度, 第3度, 第4度

ミ4つに致して居ります，2つに分けた人もあり5つに分けた人もあります．これは度分けの數の多い程その正確さが失はれて行くものでありますから，もしも分けるのなら私は *v. Hansemann* の最初に試みたように3つに分ける位で滿足する方がよいミ考へてゐます．多くの度に分けるこミは臨牀上の實際に應用して全く意味のない無益の企で，唯學者の獨りよがりに過ぎないやうな氣がします．

尙ほ表の最後の列にあります＋，－の符號は研究者が組織學的の度分けミその豫後ミを比較考察した結果組織學的の度分が癌腫の惡性の程度に一致するミいふ成績を得たものに＋．一致せずミいふ成績を得たものを－にして示してあるのでありまして，否定的の成績が少數であるこミは注意す可きこミであります．

今この表に掲げて置いた多數の業績の中から特色のあるものを選んで述べて見るミ，*Broders* 竝びにその共同作業者のものを除いて，その他のものゝ中で先づ *Broders* の先輩であり初めはその指導者であつた *MacCarty* の研究(第9番)について御話し致すこミにします．彼れは癌腫の基質(結締組織)に起る變化に重きを置いて，基質に圓形細胞の浸潤や，結締組織の纖維化乃至硝子化が著明に現はれてゐる程度の強い程その豫後の良いのを認め，是等の變化を癌細胞の發育に對する防禦的の組織反應であるミ解釋して，これを防禦的因子 (defensive factors) ミ呼びました．これには反對者が多く，彼の弟子である *Broders* の研究の方に團扇があがつたのは聊か氣の毒のやうな氣も致します．基質に於ける圓形細胞の浸潤に *MacCarty* のいふ防禦的因子ミしての意味が全く無いミは云はれないでせうが，癌の實質に壞死が著しく現はれる場合にこれが強く起るこミは屢ゝ認められてゐる所でありますので，*MacCarty* の云ふ樣な議論は成立しないのであります．

私は表に掲げた多數の研究報告の中で群を抜いて最も優れてゐるミ思ふものは *Haagensen* の乳癌についての研究(第 39 番)であります．彼れはその前に發表せられた *Greenough* の乳癌についての研究(第 14 番)の考案を一層廣くし確實のものにしたのでありまして，癌細胞の分化の程度ミ云ふやうな一本調子の議論ではなく，色々の所見を一つ一つ取りあげ，その變化の程度ミ豫後ミを比較して見た上で，無關係のものはこれを棄て，殘りのものゝ中で何れの變化を最も重要視す可きものであるかミいふこミを精しく研鑽したのであります．あミから私が述べやうミ考へてゐる度分けの標準はこの研究成績を基ミし其他のものを參考して正しいミ考へる所を綜合したものであります．

それから主に佛國で行はれた研究に見るのでありますが，*Delbet & Mandars* が乳

癌についての研究(第 20 番)に於て,「ムチカルミン」を用ひて癌組織切片中の粘液を染色し,粘液の出現の多いもの程豫後が良いと報告してゐるのであります.これはその後 *Bertrand & de Nagy* との研究(第 32 番)によつて否定せられてゐますが,*Mureau & Lambert* との研究(第 38 番)によつて肯定せられたのでありますから,あながち棄てたものでは無いと考へます.

最後に極端な度分けをやつた研究を紹介致します.それは *Heuper & Schmitz* の業績(第 16 番)であります.私は不幸にしてその原著を讀む機會を得ませんので,抄錄の受け賣りでありますが,悪性度に關係すると彼れが推定した組織學的事項を約20ヶ條擧げてその各々についてその重要性に從つてその悪性度を採點し,全部の事項の採點を總計して,これによつて癌腫の悪性度を決定せんとするのであります.彼れはこの採點表を組織學的悪性計(histological malignogramm)と呼んでゐますが,これには全然共鳴者を得ませんでした.

以上で大體主な文獻について述べましたが,然らば今日この問題について御前は何う考へて居るかといふ御質問がありと致すれば私は「組織學的の Anaplasie の程度は悪性度と或る點までは一致するが,これには可なり多數の例外を認めた上のことである」と答へたいのであります.これは私自身のみの獨斷ではありません.今日の病理學の常識であると斷言致して差支ないと思ひます.曾て米國でこの研究が盛に行はれた當時にニューヨーク市の *Ewing* 教授は「病理學者は癌腫といふ組織學的診斷を下す際にそのものゝ悪性度を組織學的に決定する義務がある」といふ様なことを公開の席で述べてゐますが,彼れが今日でもこの問題をそれ程重要と考へてゐるか疑問であります.又 *MacCarty* は *Haagensen* がワシントン市に於て催された米國癌研究會に前に述べました業績を發表した際に次のやうな討論を致してゐます.「第何度のものはその 80% が豫後が良かつたといふ風に述べてゐられるが,殘りの 20% は豫後が悪るかつたのでありませう.さすれば玆に組織學的に調べて第何度の癌患者ありとした時に,醫者はその豫後について何と答へてよいでせうか.その例は 80% の良い方に入れてよいか,20% の悪い方に入れてよいか決定が出來ないではありませんか」これは實に御尤もな議論である.それで結局組織が現はす Anaplasie の程度は臨牀醫が臨牀的の色々の所見を綜合してその豫後を考へる際に參考に供する價値を有するものであることは疑ひはありませんが,これのみによつて悪性度を決定するといふことはどんでも無い間違ひであると云ふことになるのであります.腫瘍の良性悪性といふことはその生物學的の性狀であります.この生物學的の性狀が全部組織學的の形

態の上に現はれてゐない場合があることは申す迄もないことであります．悪人であるのにその外觀が善人であるように見えるといふのと同じことが癌腫の組織像にも認められることを忘れてはならないと思ひます．

癌腫の特有な組織學的の構造は申す迄もなく蜂窩狀の構造(alveolärer Bau)であります．基質の中にある蜂窩の如き空隙の所に實質(癌細胞)が見出されるのを云ふのであります．これは癌細胞が組織隙中に自ら能動的に侵入しつゝ發育(浸潤性發育)するといふその悪い生物學的の性狀の一つの現はれであります．基質の一部は無論癌細胞の增殖と平行して新生するものであるから，この構造を以て既存組織中に癌腫が浸潤した像と一概にいひ切ることは出來ませんが，上皮細胞が癌細胞と變じて正常に存在す可き域を超えて異所的に他の組織內に侵入するために出來るものであることは議論の餘地がないことであります．*Beneke* は嘗てこの蜂窩(Alveolen)を充してゐる癌細胞巢(Krebszellnester)は一つ一つ別々のものでその隣のものと互につながりあつてゐないことが癌腫に特有であつて，癌性でない上皮の異型的の增殖の場合には互に連絡してゐるから容易にそれと鑑別出來る樣に云つたことがありましたが，連續切片を作つて檢べて見ると癌腫であつてもその細胞巢が互につながつてゐる所もあるので，この點では鑑別出來ないのであります．然し一つの切片標本の中で細胞巢の多くが互に連絡してゐる場合はこれを眞の蜂窩狀の構造と見做し難いもので，次に述べる網狀構造に近いものでその移行型と稱へてもよいでありませう．

尙ほ蜂窩狀の構造の認められる癌腫組織に於て癌細胞巢で充されてゐる蜂窩の或るものが血管とか淋巴管であることがあります．これは癌腫の浸潤性の破壞的の發育が血管乃至淋巴管の壁に及んでその管腔內に浸入したことを證據立て從つて癌腫の恐る可き轉移のよつて來たる所以を我々に敎へる興味ある所見であります．標本內に斯かる組織像が多く見出される場合は轉移の成立する危險も多く，從つて理論上それだけ悪性度の强いものであると想像せられないことはないのであります．然し事實に於て轉移の成立にはその他の多くの要約の併存を必要とするものでありますから，この豫想が必ずしも的中しないのであります．又それと反對に前述の血管乃至淋巴管の管內發育の組織像が容易に見出せない例について全身に多數の轉移竈を認むることがあるのは我々の日常經驗する所であります．それで私はこの所見はあまり重要視することが出來ないと考へてゐます．

網狀構造(netzförmiger Bau, plexiform structure)といふのは癌細胞巢が互につながつて網狀になり，その網の目に當る所に基質が島の樣に點々として認められるのをいふのであります．これは癌細胞が增殖する場合に前のものと異つて周圍の組織の內に自ら能動的に侵入して行く傾向が少なく，これとは反對に增殖した癌細胞群の中

へ周圍から結締組織(血管の新生を伴つて)が侵入してその基質を作る場合に出來上るものと私は考へてゐます．從つて理論上この型の構造を有するものは浸潤性の發育を營む傾向の少ないものに見られるといふことになります．癌腫の組織の一部にこの像が見らるれば全部が蜂窩狀構造を示すものよりそれだけ良性であると考へてよいと思ふのでありますが，前に述べた *Haagensen* は乳癌についての研究成績からして，これは癌腫の惡性度を定める標準にならぬと記述してゐます．この問題の解決は今後の研究に俟つことに致します．

癌細胞は異所的に浸潤性にのみ發育するとは限らず同時に又組織の表面に發育（表面的の發育）して乳嘴狀の增殖を起すことがあります．これは肉眼的にはそれ程明かではなくとも顯微鏡下にこの型の增殖を認められることが屢々あります．乳嘴腫は御承知の通り被覆上皮細胞が皮膚乃至粘膜の表面を被覆するといふ生理的の性狀を失はずに然かも腫瘍性の增殖を現した結果出來上るもので，理論的に考へても皮膚乃至粘膜が乳嘴狀にその表面に突出して，その表面の面積を廣くするより他にその增殖した上皮細胞を收容する餘地は無いのであります．然るに斯樣な良性の上皮性腫瘍と異つて，癌腫になりますと，前に述べました樣に深く組織隙に侵入して增殖(浸潤性發育)して行くのでありますが，これは被覆上皮(腺上皮については後に述べます)が組織の表面を被覆するといふ性狀を失つた結果であり，從つて又その惡性の現はれであると考へてよいのであります．初め良性であつた乳嘴腫が後に惡性化して癌腫に變ずることがありますが，その際組織學的には被覆上皮としての表面的の發育に浸潤性の發育が加はつて行くことを明に認め得るのであります．又前に述べましたやうに乳嘴腫が癌腫に變化したといふのではなく，初めから癌腫として發生したものが癌腫にのみ見られる浸潤性の發育と同時に表面的の發育を現はして，その表面に乳嘴狀の增殖を起すことがあるのであります．これは理論的の推論から行くと癌細胞は被覆細胞としての組織を被覆するといふ性狀を未だ全く失つてゐない證據でありまして，それだけ癌腫としては未だ比較的良性である，惡性度の弱いものであるといふことになるのであります．斯樣な乳嘴狀の癌腫の表層の所だけが試驗的に切除せられて，これを組織學的に檢査せられたといふような時には，生憎切除せられた部分が癌腫に特有な浸潤性の發育を現はさずに表面的の發育のみを營んでゐる所でありますから良性腫瘍としての乳嘴腫とその構造を同じくしてゐますので，それと鑑別することがむつかしくなるのであります．然しその際乳嘴狀の增殖物の表面を覆つてゐる上皮細胞は癌細胞であるのでありますから，細胞學的にこの細胞を精しく檢査すれば良性の普通の乳嘴腫の被覆

上皮とは異つてゐて色々の點に於て異型的である事がわかり，癌腫に固有な蜂窩狀の構造は證明出來ないが，多分癌腫であらふといふ組織學的の診斷は下し得るのであります．

以上便宜上乳嘴狀の表面的の發育を述べましたが，同樣な發育の形式は腺管內にも行はれるのであります．私はこれも亦表面的發育の一型であると考へてよいと思ひます．腺管の內腔に向ふ所を組織の表面と考へますと，癌細胞がその管腔內で增殖（腺管內發育）することは組織隙に浸潤性の發育を營むのとはその組織に對する態度は同じでないのであります．被覆上皮から發生した癌腫も腺管內發育を現はすことがあるが，腺上皮から發生した癌腫がその腺組織內に發育し行くと至る所に腺管があるので容易にその內に侵入して，腺管內發育を起すことになります．時にはこの型の發育が全く主となつてゐるのが認められることもあります．*Haagensen* は乳癌について腺管內發育を營むものは比較的良性であるといつてゐます．私は乳嘴狀の增殖を營む癌腫が比較的良性であるといふ議論がそのまゝこの腺管內發育をなす癌腫にもあてはまるのであると考へてゐます．それは何れも癌細胞の增殖が主として表面的に行はれて浸潤性の發育をする傾向が少ないからであると解釋したいのであります．

以上は發育の形式に基く癌腫組織全體の構造を組織學的に見てその惡性度について御話し致したのでありますが，次に蜂窩內に於ける癌細胞巢そのものの構造に就て考へて見たいと思ひます．被覆上皮から發生した癌腫の癌細胞巢ではその中心部が元來の被覆上皮の表層面に當り，基質に接する周邊部が被覆上皮の基底層に當るのであるから，癌細胞として上皮の分化が失はれてゐない場合には扁平上皮癌（類癌）ではその癌細胞巢の中心部には角化層（癌眞珠）があり，それにつゞいて棘細胞層があり，周邊部には基底層が認められて，生理的にこの細胞は分化の結果當然角化す可き性狀を其儘現はすことになります．然るにこの分化の現像が減退すると癌眞珠の形成が認められなくなるばかりでなく，棘細胞も不明となり，基底細胞のやうな形態の細胞だけから癌細胞巢が出來てゐる例（基底細胞癌）も出來て來るし，又尙ほ一層退化すると癌細胞巢が基底細胞とも稱へ兼ねる不定型の幼若な細胞から形成されるといふ風にその退化の程度に從つて癌細胞巢の構造が異つて來る．これは卽ち *Hansemann* の始めから主張してゐる所で大體退化の程度によつて惡性度が推察せられるのであります．

圓柱上皮癌についても同樣にその癌細胞巢の構造によつてAnaplasieが決定せられるのであります．圓柱上皮癌は癌細胞巢には腺樣の構造が認められその中心に管腔を認めると同時にこの管腔をとりまいてゐる圓柱上皮の配列が生理的の圓柱上皮に比較

的類似したものが最も退化してゐない他の語を以てすればAnaplasieの强くない比較的良性のもので，その圓柱上皮の形態が不正になるに共にその配列も異型的になり，終にはその管腔をも失ふに至る迄の退化の程度によつてAnaplasieの程度を定めるのであります．

最後に一つ一つの癌細胞について觀察するに何んな癌であつてもその核や細胞體の形態に不同がありその大さも一樣でないが，退化が進むに從つてこの多態症(Polymorphie)が著明になる．これによつてAnaplasieの程度を推定する一つの標準にすることが出來ます．

細胞の大きい方が小さいものより惡性であるといふ人もありますが，これは多態症があつて細胞の大さが不同でその中に大きな細胞が混つてゐるのが惡性であると解す可きであります．それから核の染色質が增加して「ヘマトキシリン」で濃染するものが多く現はれて來る．この過色症(Hyperchromasie)の程度も亦Anaplasieの標準にすることが出來るのであります．尙癌細胞の盛んな增殖の一つの現はれとして分裂期に於ける細胞が證明されることであります．これは組織標本內に於ける核分剖像として容易にこれを認め得るものでありますから，これも亦惡性度を決定するに當つての一つの目標となります．その數が多い程その增殖がそれだけ盛であつたといふことになり癌の發育が早くて惡性であるといふことになるのでありますが，可なり發育の旺盛の癌腫でもこれを組織學的に調べて見ると，稀期に反して僅少の核分剖像が證明されることがあります．核分剖像は細胞分裂の途中に認められる各瞬間の像でありますから，これは癌腫の組織が固定せられた瞬間に核分剖が少なかつたといふに過ぎません．それですから核分剖像が多い場合に癌の發育の早いことに從つてその惡性であることを想像して差支ないですが，見られないからといつて常に比較的良性であるとは推定出來ないのであります．

癌細胞にその發生母地の上皮細胞が持つてゐた生理的の機能が全く失はれることなく保たれてゐることがあります．生理的の機能が退化が進むに共にそれは認められなくなるといふことは理の當然であるので，形態學的に生理學的の機能の存在を證明し得れば，それだけ理論上Anaplasieの程度は弱いといふことになるのであるが，何うも惡性度の標準としてこれに重きを置くことは出來ないやうに考へてゐます．例へば胃腸の粘膜から發生する圓柱上皮癌に粘液變性が現はれることがある．その高度なものは膠樣癌と稱せられるわけであるが，この粘液變性たるや元來胃腸粘膜の被覆上皮(*Lieberkühn*腺と稱せられる部分もこの被覆上皮を以て覆はれた粘膜表面の凹みに過

ぎないのである）には多數の杯細胞があつて生理的に粘液が分泌せられてゐるのであるから，この被覆上皮が生理的の粘液を作るといふ形態を保つたまゝで癌腫となれば，癌腫内に粘液が出來るのは當然であることになるのである．この膠樣癌は比較的良性であるために，癌腫が可なり大きくなる迄患者が生命を保ち得ることは一般に認められた所であります．又肝細胞癌（實質性肝癌，「ヘパトーム」）に膽汁の分泌があるために癌腫の實質に黄疸が現はれてゐることがあります．然しこの場合膽汁の分泌のために黄疸の起つてゐる例と，然らざる例との間にその惡性度に於て著しい相異を認め得ないやうであります．尚その他の場合を合せて廣く考察して見ると，幾分か標準になれと思はれることも無いではないが，大體に於て餘りあてにならぬ樣であります．これは細胞の機能を我々が形態學的に證明し得るのは不幸にも僅かにその一小部分に過ぎないためではないかと考へます．

以上で大體私の癌腫の惡性度に關する考への大體を御話し致しましたが，私は自分の經驗からして，組織學的に惡性度の度分けをするといふことは，未だそれより先に癌腫であるといふことが確實に決定せられた上に行はれるいはゞ餘裕があつてのことであると思ひます．この理由からして私は惡性度の決定といふことは臨牀上それ程重要な問題であるとは考へてゐないのであります．それだといつて腫瘍病理學上のこの種の研究を決して輕視するわけでありまんから誤解のなき樣御願ひを致して置きます．事實組織學的に確實に癌腫であるといふ診斷を下すには深甚なる考慮を要するものであります．

癌腫であるかどうか確かでないものを誤つて所謂第一度の癌腫であると診斷すれば癌腫ならざるものを癌腫の中に加へたのですからその豫後が良いのは當然で，それであるから第一度の證明が出來たとは申せません．私はこの誤診のために癌腫ならざるものが癌腫として手術せられた實例を知つてゐます．

癌腫の中には先天性の發育異常（組織畸形）によつて出來た腫瘍芽から發生するものもありますが（異個體發生性腫瘍 dysontogenetische Geschwülste），その多數は生理的の上皮組織が後天性に增殖する間に發生するものである（過形成元腫瘍 hyperplaseogene Geschwülste）．從つてこの發生期に屬するものを我々が見ることがある．今日に於ては動物に人工的に癌腫を發生せしめ得るのであるから，我々は臨牀材料や解剖材料で偶然これを見出すのみならず，實驗動物からもこれを容易に求め得るやうになつてゐるのであります．これ等の材料から得た經驗から考へて見ますと，發生期乃至初期の癌腫に向つて所謂第一度の癌腫といふ診斷（殊に試驗的切除組織片によつ

ての組織學的診斷)が下される恐れが大にあるこ考へるのであります.

西歷1877年 *Friedländer* は炎症その他の場合にその組織に癌腫に似たる『異型的上皮增殖』(atypische Epithelwucherung)が認められゝこゝを注意しました. 彼れはこの術語を以て非癌腫性の增殖を意味してゐるのでありますが, 癌腫の發生期のものに就て我々が學び得た所から考へますこ, 上皮に現はれた非癌腫性の增殖が漸次に癌腫性に變つて行く場合に, その移行は極めて徐々に行はれるもので, いつ變つたこもなく段々に移つて行くのでありますから, これまでが異型的上皮增殖で, これからが癌腫性の增殖であるこいふやうな明かな境界があるわけではないのであります. それで私はこれ等の上皮の異型的增殖を全體一つにまこめて取扱つた方が合理的であるこ考へましたので, 異型的上皮增殖を廣義に解してこれ等全部を異型的上皮增殖こ呼ぶこゝに致してゐます.

1. 癌には成らぬ異型的の上皮增殖
2. 癌に成る前の異型的の上皮增殖
3. 癌に成りつゝある異型的の上皮增殖
4. 癌に成りきつた異型的上皮增殖

私共は常にこの4つの異型的の上皮增殖があり, 而かもそのものが順次に移行し得るものであるこゝを心にこめた上で, 癌腫の組織學的診斷に從事す可きであるこ考へます. この中で特に第2の前癌性の上皮の異型的增殖は各臟器についてそれぞれ已に記載せられてゐる特殊な變化があるのでありますから, それ等についての知識も亦確實なる診斷を下す上に於て缺く可からざるものであります. 殊に癌腫の早期診斷には斯かる考察を缺いた診斷は何等の價値を有せざるものであるこゝを御注意申上げたいのであります.

最後にもう一言申し添へたいこゝがあります. 私共が臨牀的に小さな切除組織片について癌腫の組織學的診斷を下します場合に, 殘念ながら常に必ずしも「確かに癌腫なり」或は「癌腫に非ず」こ云ふ樣に明かに答へ得るこは限らないのであります. 若し假に玆に病理學者があつて, 常に明白なる答を與へ得るこ考へてゐるこすれば, 彼れは自からを欺くものか, 或は知識經驗の不足なるものであります. 「確かに癌腫なり」, 或は「確かに癌腫にあらず」こ答へ得る他に「多分癌腫なり」, 「多分癌腫にあらず」, 「癌腫なるや癌腫ならざるや明かならず」こ答へざるを得ざる3つの場合あるを私は自から經驗してゐるのであります. そしてこの診斷の確かさの程度を臨牀醫に知らしめる方が治療の方針を定める際に一層參考こなるものであるこ信じてゐるのであります.

それで私はこの診斷の確かさの程度を次の如き符號を以て現はすのが便利であらうと考へこれを實行してゐます．「確かに癌腫なり」を＋を以て，「多分癌腫なり」を＋？を以て，「癌腫なるや癌腫ならざるや明かならず」を±を以て，「多分癌腫にあらず」を－？を以て，「確かに癌腫にあらず」を－を以て標示するのであります．而して－？の場合には組織的檢査によつて癌腫の診斷を下すに足る所見が全然認められないが，さればといつて全く陰性であると否定してしまふ事は出來なかつたのでありますから，臨牀的に今後の經過を注意して觀察する必要あることを臨牀醫の方に御警告もし希望もしてゐるのであります．それから±の場合は再檢査を要する場合でありまして，僅か1回の檢査の所見を以て不確實な診斷を下すことを勉めて避け，必ず再檢査を行ひ前後2回の所見(必要ある時には3,4回の所見)を合せてより確實な診斷を行はねばなりません．＋？の場合は組織學的には可なり癌腫の疑ひは濃厚であるが，組織學的の所見だけからして癌腫と斷定することが出來なかつたのでありますから，その場合臨牀的に癌腫といふことが確かに認め得らるるなれば，無論癌腫としての治療を直ちに始むべきであります．然し若し臨牀的にも癌腫の疑ひといふ程度のものなれば，組織學的の再檢査を怠つてはなりません．この程度のものが誤つて癌腫として無用の治療を受けることがあるからであります．斯くの如くにして組織學的檢査の結果が臨林治療上正しく利用せらるることになるのであります．

本講演に要した文獻の調査，幻燈寫眞の製作その他について，瀧澤，藤原兩氏を煩はしたことに對して茲に厚き感謝の意を表してこの講演を終ることに致します．

References

1) *Balfour*, Curability of cancer of the stomach, Collected Papers of the Mayo Clinic and the Mayo Foundation 23: 80, 1931. 2) *Bertrand* and *de Nagy*, Recherches sur quelques tests concernant le pronostic histologique de cancers du sein, Presse méd. 39: 991, 1931. 3) *Boss*, Der Wert der pathologisch-anatomischen Untersuchung für die Prognose des Brustdrüsenkrebses, Beiträge zur klinischen Chirurgie 121: 642, 1921. 4) *Broders*, Squamous-cell epithelioma of the lip, a study of 537 cases, Journal of the American Medical Association, March 6, 1920. 5) *Broders*, Cancers self-control, Collected Papers of the Mayo Clinic and the Mayo Foundation 16: 1165, 1924. 6) *Broders*, Squamous-cell epithelioma of the skin, a study of 256 cases, Annals of Surgery 73: 141, February No. 2, 1921. 7) *Broders*, Epithelioma of genito-urinary organs, a study of 473 cases, Annals of Surgery 75: 574, 1922. 8) *Broders*, Epithelioma of the cavities and internal organs of the head and neck, Archives of Surgery, 11: 43, 1925. 9) *Broders*, The Grading of carcinoma, Collected Papers of the Mayo Clinic and the Mayo Foundation 17: 973, 1925. 10) *Broders*, The grading of cancer and its practical application, Col-

lected Papers of the Mayo Clinic and the Mayo Foundation 18: 1180, 1926. 11) *Broders*, Carcinoma of the mouth types and degrees of malignancy, American Journal of Roentgenology and Radium Therapie 17: 90, 1927. 12) *Broders* and *Vinson*, The degree of malignancy of carcinoma of the oesophagus, Collected Papers of the Mayo Clinic and the Mayo Foundation 20: 10, 1928. 13) *Crenshaw*, Observation on malignant epithelial neoplasms of the Bladder, Collected Papers of the Mayo Clinic and the Mayo Foundation 17: 380, 1925. 14) *Dahl-Inversen*, Examen ulterieur de 109 malades ayant subi l'opération radicale du cancer du sein, concernant essentiellement le rapport entre la découverte microscopique et la fréquence de la récidive, Lyon chirurg. 24: 648, 1927. 15) *Delbet* and *Mandaro*, Les cancers du sein, Paris Massons et Cie, 1927. 16) *Feist* und *Bauer*, Zur Statistik des Brustkrebses, Beiträge zur klinischen Chirurgie 125: 636, 1922. 17) *Flothow*, Defensive factors in carcinoma of the breast, Surg., Gynec. and Obst. 46: 789, 1928. 18) *Greenough*, Varying degrees of malignancy in cancer of the breast, The Journal of Cancer Research 9: 453, 1925. 19) *Haagensen*, The Bases for the histolgic gradig of carcinoma of the breast, The American Journal of Cancer 19: 285, 1933. 20) *Halstead*, The results of radical operations for the cure of cancer of the breast, Annals of Surgery 46: 1, 1907. 21) *Hansemann*, Über die Anaplasie der Geschwulstzellen und die asymmetrische Mitose, Virchows Archiv 129: 436, 1892. 22) *Hansemann*, Studien über die Specifität, den Altruismus und die Anaplasie der Zellen, A. Hirschwald, Berlin, 1893. 23) *Hansemann*, Die mikroskopische Diagnose der bösartigen Geschwülste, A. Hirschwald, Berlin, 1902. 24) *Heuper* and *Schmitz*, Relations of histological structure and clinical grouping to the prognosis of carcioma of the breast and uterine cervix, Annals of Surgery 81: 993, 1925. 25) *Hoffmann*, Die Therapie des Mammacarcinoms und ihre Erfolge, Beiträge zur klinischen Chirurgie 121: 400, 1921. 26) *Judd* and *Baumgartner*, Malignant lesions of the gallbladder, Collected Papers of the Mayo Clinic and the Mayo Foundation, 21: 147, 1929. 27) *Lee* and *Stubenbord*, Clinical index of malignancy for carcinoma of breast, Surg., Gynec. and Obst. 47: 812. 1928. 28) *Leroux* and *Perrot*, Pronostic histologique des cancers du sein, Bull. de l'Assoc. franç. p. létude du cancer 19: 439, 1930. 29) *Lindenberg*, Zur Statistik der operativen Dauerheilungen des Mammacarcinoms, Deutsche Zeitschrift für Chirurgie 128: 156, 1914. 30) *MacCarty*, Clinical suggestions based upon a study of primary, secondary(carcinoma?) and tertiary or migratoty (carcinoma) epithelial hyperplasia in the breast, Surg., Gynec. and Obst. 18: 284, 1914. 31) *MacCarty*, A biological conception of neoplasia, its terminology and clinical significance, American Journal of Medical Sciences 157: 657, 1919. 32) *MacCarty*, Factors which influence longevity in cancer, Annals of Surgery 76: 9, 1922. 33) *Mahle*, The morphological histology of adenocarcinoma of the body of the uterus in relation to longevity, Surg., Gynec. and Obst. 36: 385, 1923. 34) *Martzloff*, Carcinoma of the cervix uteri; a pathological and clinical study, with particular reference to the relative malignancy of the neoplastic process as indicated by the predominant type of cancer, Bulletin of the Johns Hopkins Hospital 34: 141, 184, 1923.

35) *Mureau* and *Lambert*, Les facteurs de malignité dans les cancers du sein, Cancer, Bruxelles, 9: 117, 1932. 36) *New*, Thyrotomy for carcinoma of the larynx, Collected Papers of the Mayo Clinic and the Mayo Foundation 23: 777, 1931. 37) *Ngai*, The etiological and pathological aspects of squamous-cell carcinoma of the penis among the Chinese, The American Journal of Cancer 19: 259, 1933. 38) *Partey* and *Scarff*, The position of histology in the prognosis of carcinoma of the breast, Lancet 1: 801, 1928. 39) *Pemberton* and *Fricke*, Treatment of carcinoma of the thyroid gland, Collected Papers of the Mayo Clinic and the Mayo Foundation 23: 575, 1931. 40) *Plaut*, The relation between the histologic picture and the prognosis of tumors, Archiv Path. and Lab. Med. 3: 240, 1927. 41) *Rankin* and *Broders*, Factors influencing prognosis in carcinoma of the rectum, Collected Papers of the Mayo Clinic and the Mayo Foundation 19: 387, 1927. 42) *Reimann*, The issues at stake in the grading of tumors, Archives of Path. 8: 803, 1929. 43) *Salomon*, Beiträge zur Pathologie und Klinik der Mammacarcinome, Archiv für klinische Chirurgie 101: 573, 1913. 44) *Sistrunk* and *MacCarty*, Life expectancy following radical amputation for carcinoma of the breast; a clinical and pathologic study of 218 cases, Annals of Surgery 75: 61, 1922. 45) *Smith* and *Bartlett*, Malignant tumours of the female breast, Surg., Gynec. and Obst. 48: 314, 1929. 46) *Stewart*, Radiosensitivity of tumors, Laboratory studies Vol. XIV and Clinical studies Vol. X from Memorial Hospital, 1933. 47) *Vinson*, Primary carcinoma of the bronchus; Report of seventy-one cases in which the diagnosis was made by bronchoskopic examination, Collected Papers of the Mayo Clinic and the Mayo Foundation 23: 884, 1931. 48) *Warren*, The grading of carcinoma of the cervix uteri as checked at autopsy, Archives of Pathology, 12: 783, 1931. 49) *Warren*, Studies on tumor metastasis, Surg., Gynec. and Obst. 56, 742, 1933. 50) *Watson*, Carcinoma of oesphagus, Laboratory studies Vol. XIV and Clinical studies Vol. X from Memorial Hospital, 1933. 51) *White*, Late results of operation for carcinoma of the breast, Annals of Surgery 86: 695, 1927.

第三十卷第四號正誤表

食道癌の「ラヂウム」療法(第一報)

山下久雄

頁　行	誤	正
510頁 4行	せざる_からず.	せざるべからず.
511頁 2行	多きものなり.	多きことなり.
515頁 第二圖	Die Radonseeds in d. rechten Supraelaviculardiüsenmetastasenen	Radonsamen in d. rechten Supraclaviculardrüsenmetastasen
516頁 第五表	Reportern	Autoren
516頁下ヨリ2行	極めて多重……	極めて多量……
518頁 第五圖	10 mg「ラヂウム」管2本……	10 mg「ラヂウム」管3本……
519頁 第六表	Rádon	Radon
526頁 18行	食部中央上部	食道中央上部
530頁 17行	struation	stration
530頁 28行	Roent. u. Rad.	Roent. & Rad.
530頁 32行	Ösophagusca.	Ösophagusca.,

Berichtigung.

In dem Aufsatz von Ichiro Otsuka und Naoaki Nagao (Band 30, S. 561, 9. u. 10. Zeile v. u.) sind statt der Worte „von mutmassliche Substanz“ die Worte „von mutmasslichen Substanzen“ einzusetzen.

財團法人 癌研究會寄附行爲

昭和八年十一月十七日設立許可

昭和八年十二月 一 日法人登記

第一章 總 則

第一條 本會ハ財團法人癌研究會ト稱ス

第二條 本會ハ癌其他ノ腫瘍ニ關スル研究及研究ノ奬勵竝ニ其豫防治療ヲ爲スヲ以テ目的トス

第三條 本會ハ前條ノ目的ヲ達スル爲メ研究所及其附屬病院ヲ設置シ又ハ學術集談會ノ開催、優秀業績ヘノ授賞、研究費ノ補助、圖書雜誌ノ發行、國際的對癌運動ノ參加若クハ豫防知識ノ普及其他ノ施設ヲ爲ス仍必要ナル企劃ハ評議員會ノ議決ヲ經テ之ヲ定ム

前項ノ研究所及附屬病院、集談會、授賞、補助竝ニ圖書雜誌ノ發行等ニ關スル規定ハ別ニ之ヲ定ム

第四條 本會ハ事務所ヲ東京市豐島區西巢鴨二丁目二千六百拾五番地ニ置ク

第二章 資産及經費

第五條 本會ノ資産ハ左ノ如シ

一、社團法人癌研究會ヨリ寄附ヲ受ケタル別紙目錄記載ノ財産

二、後援會其他ノ者ヨリノ寄附ニ依ル金品

三、帝國政府ノ補助金

四、其他ノ收入

第六條 本會ハ左ノ財産ヲ基本財産トス

一、前條第一號ノ財産

二、前條第二號ノ寄附金品、但シ用途ヲ指定シテ寄附シタル金品ハ此ノ限ニアラズ

三、繰越金中評議員會ニ於テ基本財産ニ編入スヘキコトニ議決シタル金圓

第七條 基本財産ハ費消スルコトヲ得ス但シ臨時必要ナル場合ニハ評議員會ノ議決ヲ經テ經常費又ハ當該ノ費目ニ繰入ルルコトヲ得

第八條 基本財産ハ國債證券又ハ確實ナル有價證券ヲ買入レ若クハ郵便官署又ハ確實ナル銀行、信託會社ニ預入レテ保管ス資産ノ管理ニ關スル細則ハ評議員會ノ議決ヲ經テ別ニ之ヲ定ム

第九條 本會ノ經費ハ左ニ揭クルモノヲ以テ支辨ス

一、基本財産ヨリ生スル收益

二、帝國政府ノ補助金

三、用途ノ指定アリタル寄附金

四、繰越金中基本財産ニ編入セサル金圓

五、其他ノ收入

第十條 本會ノ會計年度ハ每年四月一日ニ始マリ翌年三月三十一日ニ終ル

第十一條 本會ノ豫算及ビ決算ハ評議員會ノ議決又ハ承認ヲ經ルコトヲ要ス

必要アルトキハ評議員會ノ議決ヲ經テ別途特別會計ヲ設クルコトヲ得

第十二條 年度末決算ニ剩餘金ヲ生シタルトキハ之ヲ翌年度ニ繰越ス但シ評議員會ノ議決ヲ經テ之カ一部若ハ全部ヲ基本財産ニ編入スルコトヲ得

第三章 總裁及顧問

第十三條 本會ニ總裁一名ヲ推戴ス

第十四條 本會ニ副總裁二名ヲ置ク

第十五條 本會ニ名譽顧問及顧問若干名ヲ置ク

第十六條 副總裁ハ總裁之ヲ囑託シ、名譽顧問ハ左記ノ者ニ對シ總裁之ヲ囑託ス

一、主務大臣

二、評議員會ニ於テ推薦シタル者

第十七條 顧問ハ理事會ノ推薦ニ依リ總裁之ヲ囑託ス顧問ハ本會ノ諮問ニ答フ

第四章 役 員

第十八條 本會ニ左ノ役員ヲ置ク

會　頭	一　名
副會頭	二　名
理事長	一　名
理　事	十　名以上 十五名以上
監　事	五　名以內
評議員會長	一　名
評議員	若干名

第十九條　理事及監事ハ評議員會ニ於テ之ヲ選擧ス

第二十條　會頭、副會頭及理事長ハ理事中ヨリ互選ス但シ會頭又ハ副會頭ハ時宜ニ依リ理事長ヲ兼ヌルコトヲ得

第二十一條　評議員會長及評議員ハ會頭之ヲ囑託ス

第二十二條　會頭ハ本會ヲ統轄シ評議員會ヲ除ク外學術集談會其他ノ會議ノ議長トナル副會頭ハ會頭ヲ補佐シ會頭事故アルトキハ之ヲ代理ス

第二十三條　理事長ハ本會ヲ代表シ會頭ノ旨ヲ受ケテ一切ノ會務ヲ處理ス

理事長事故アルトキハ豫メ理事長ノ定メタル順序ニ依リ他ノ理事代テ其職務ヲ行フ

理事長ハ理事會ノ議決ヲ經テ有給ノ書記若干名ヲ置クコトヲ得

第二十四條　監事ハ本會ノ會計及資產ヲ監査ス

監事必要アリト認メタルトキハ評議員會ノ招集ヲ要求スルコトヲ得

第二十五條　評議員ハ評議員會ヲ組織シ本會樞要ノ事項ヲ評議ス

評議員會ハ必要ニ應シ會頭之ヲ招集ス評議員半數以上ノ同意ヲ以テ評議員會招集ノ請求アリタルトキ及前條第二項ニ依リ監事ヨリ請求アリタルトキ亦同シ

第二十六條　評議員會長ハ評議員會ノ議長トナル評議員會長事故アルトキハ會頭ノ指定シタル評議員之ヲ代理ス

第二十七條　評議員會ノ招集ハ會議ノ目的タル事項、日時、場所ヲ指示シテ開會七日前ニ各評議員ニ招集ノ通知ヲ發スヘシ但シ會頭ニ於テ緊急必要アリト認メタル場合ハ此限ニアラス

第二十八條　評議員會ニ出席スルコト能ハサル評議員ハ書面ヲ以テ表決ヲ爲シ又ハ他ノ評議員ニ其代理ヲ委任スルコトヲ得

評議員會ニ出席ノ評議員並ニ前項ノ書面表決及代理表決ノ數カ全員ノ半數以上ニ達スルニ非サレハ議決スルコトヲ得ス

評議員會ノ議事ハ過半數ヲ以テ之ヲ決ス可否同數ナルトキハ議長ノ決スル所ニ依ル

第二十九條　役員ノ任期ハ各三年トス但シ再任ヲ妨ケス

役員ニ缺員ヲ生シ會頭必要アリト認メタルトキハ評議員會ニ諮リ第十九條乃至第二十一條ノ規定ニ依リ各其補缺員ヲ定ム

補缺員ノ任期ハ前任者ノ殘任期間トス

第三十條　役員ノ任期滿了シタル場合ニ於テモ其後任者ノ就任スルマテハ仍前任者ニ於テ其職務ヲ行フ

第五章　附　則

第三十一條　社團法人癌研究會ニ於テ推薦シタル名譽會員ニ對シテハ本會ニ於テモ亦其ノ待遇ヲ承繼ス

第三十二條　本會ノ目的ヲ翼贊スル爲メ別ニ後援會ヲ設立スルコトアルヘシ

後援會ノ名稱其他必要ナル規定ハ別ニ之ヲ定ム

第三十三條　本寄附行爲ノ條項ヲ變更セントスルニハ評議員四分ノ三以上ノ同意ヲ得主務官廳ノ認可ヲ經ルコトヲ要ス此場合第二十六條ノ規定ヲ準用ス

第三十四條　本會設立ノ際ノ役員ハ設立者之ヲ選任ス

前項ノ役員就任スルマテハ設立者其職務ヲ行フ

東京市豐島區西巢鴨二丁目二千六百十五番地
財團法人
癌研究會
事務所
電話大塚 三〇五一番 三〇七八番 四〇三二番

投稿規定

一、原稿は腫瘍に關する原著，又は豫報であつて，既に他の雜誌に掲載されたものでないことを要します.

二、寄稿者は本會會員(後援康樂會會員)に限ります.

三、原稿の採否は當方にお任せ下さい．場合により著者の了解の下に原稿の一部を短縮することがあります．登載された原稿(圖版及び插入圖をも含みます)は特に御希望なき限りは返却致しません.

四、原著の原稿は成る可く歐文(英，獨，佛語)で書き，邦文抄錄を附して下さい．邦文で原著を書かれる場合には，冗長に流れない樣に，出來る丈け簡潔に書き，歐文抄錄を必らず附して下さい．地名，人名等は原語でお書き下さい.

圖版には必らず歐文の說明をお附け下さい.

五、本誌二〇頁以內の原稿は無料で掲載します．其れ以上の頁數のものは超過分の實費だけ著者の負擔となります.

六、寫眞圖版は二頁まで無料，其れ以上は實費負擔のこと.

色刷圖版の費用は特別の場合を除き全部著者の負擔となります．圖版の大きさに關し特別の御希望がある時は其の旨御記入下さい.

七、別刷を御入用の節は其の部數を原稿の初頭に朱書して下さい．五〇部迄は無料で差上げます．其れ以上は實費負擔のこと.

八、校正は當方で致します．著者自身校正を御希望の節は其の旨原稿の初頭に朱書して下さい．尙組方の體裁は當方に御一任下さい.

九、宛名　東京市豐島區西巢鴨二丁目二六一五癌研究會

附記，本誌は每年二月末日，四月末日，六月末日，八月末日，十月末日，十二月末日に發行します．從つて，原稿受付締切は，十二月末日，二月末日，四月末日，六月末日，八月末日，十月末日とします.

財團法人癌研究會
雜誌「癌」編輯部